Baskar
09/579383

-key terms

FILE 'REGISTRY' ENTERED AT 10:21:51 ON 29 MAR 2002
E CHITINASE/CN 5
L1 435 S CHITINASE ?/CN

FILE 'CAPLUS' ENTERED AT 10:22:07 ON 29 MAR 2002
L2 16 S (L1 OR CHITINASE) AND (PLASMODIUM OR FALCIPAR?)

L2 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:150653 CAPLUS
TITLE: Monoclonal antibody against the **Plasmodium falciparum chitinase**, PfCHT1, recognizes a malaria transmission-blocking epitope in **Plasmodium** gallinaceum ookinetes unrelated to the **chitinase** PgCHT1
AUTHOR(S): Langer, Rebecca C.; Li, Fengwu; Popov, Vsevolod; Kurosky, Alexander; Vinetz, Joseph M.
CORPORATE SOURCE: World Health Organization Collaborating Center for Tropical Diseases, Department of Pathology, University of Texas Medical Branch, Galveston, TX, 77555, USA
SOURCE: Infection and Immunity (2002), 70(3), 1581-1590
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To initiate invasion of the mosquito midgut, **Plasmodium** ookinetes secrete **chitinases** that are necessary to cross the chitin-contg. peritrophic matrix en route to invading the epithelial cell surface. To investigate **chitinases** as potential immunol. targets of blocking malaria parasite transmission to mosquitoes, a monoclonal antibody (MAb) was identified that neutralized the enzymic activity of the sole **chitinase** of **Plasmodium falciparum**, PfCHT1, identified to date. This MAb, designated 1C3, previously shown to react with an apical structure of P. **falciparum** ookinetes, also reacts with a discrete apical structure of P. gallinaceum ookinetes. In membrane feeding assays, MAb 1C3 markedly inhibited P. gallinaceum oocyst development in mosquito midguts. MAb 1C3 affinity isolated an .apprx.210-kDa antigen which, under reducing conditions, became a 35-kDa antigen. This isolated 35-kDa protein cross-reacted with an antiserum raised against a synthetic peptide derived from the P. gallinaceum **chitinase** active site, PgCHT1, even though MAb 1C3 did not recognize native or recombinant PgCHT1 on Western blot. Therefore, this affinity-purified 35-kDa antigen appears similar to a previously identified protein, PgCHT2, a putative second **chitinase** of P. gallinaceum. Epitope mapping indicated MAb 1C3 recognized a region of PfCHT1 that diverges from a homologous amino acid sequence conserved within sequenced **chitinases** of P. berghei, P. yoelii, and P. gallinaceum (PgCHT1). A synthetic peptide derived from the mapped 1C3 epitope may be useful as a component of a subunit transmission-blocking vaccine.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:936235 CAPLUS

DOCUMENT NUMBER: 136:198522
TITLE: Identification of novel **Plasmodium** gallinaceum zygote- and ookinete-expressed proteins as targets for blocking malaria transmission
AUTHOR(S): Langer, Rebecca C.; Li, Fengwu; Vinetz, Joseph M.
CORPORATE SOURCE: WHO Collaborating Center for Tropical Disease, Department of Pathology, University of Texas Medical Branch, Galveston, TX, 77555, USA
SOURCE: Infection and Immunity (2002), 70(1), 102-106
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The development of transmission-blocking vaccines is one approach to malaria control. To identify novel **Plasmodium** zygote- and ookinete-secreted proteins as targets of blocking malaria transmission, monoclonal antibodies (MAbs) were produced against parasite-secreted proteins found in **Plasmodium** gallinaceum ookinete culture supernatants. Four MAbs-1A6, 2A5, 2B5, and 4B6-were identified that bound to P. gallinaceum zygotes and ookinetes in diverse patterns in terms of spatial localization on parasites, time course of antigen expression, and Western immunoblot patterns. MAbs 2A5 and 4B6 recognized more than one protein band as detected by Western immunoblot of P. gallinaceum ookinete supernatants. Beginning at 0 h postfertilization, MAb 2A5 recognized a diverse set of antigens; at 10 h postfertilization, MAb 4B6 recognized several antigens as well. MAb 1A6 recognized a single .apprx.17-kDa protein, and 2B5 recognized a single .apprx.32-kDa protein at 15 h postfertilization. In membrane feeding assays to assess the effect of these MAbs on P. gallinaceum infectivity for Aedes aegypti mosquitoes, the addn. of MAbs 1A6 and 2B5 to infectious blood meals significantly inhibited oocyst development in the mosquito midgut. In contrast, MAb 2A5 seemed to enhance infectivity. These results demonstrate that **Plasmodium** ookinetes secrete proteins (in addn. to previously characterized **chitinases**) that may be targets for blocking malaria transmission. Future investigation of ookinete-secreted neutralization-sensitive mols. should provide valuable insight into mechanisms by which ookinetes exit the blood meal, penetrate and transverse the peritrophic matrix, and invade the mosquito midgut epithelium.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:506637 CAPLUS
DOCUMENT NUMBER: 135:177745
TITLE: **Plasmodium** ookinete-secreted **chitinase** and parasite penetration of the mosquito peritrophic matrix
AUTHOR(S): Langer, Rebecca C.; Vinetz, Joseph M.
CORPORATE SOURCE: WHO Collaborating Center for Tropical Diseases, University of Texas Medical Branch, Galveston, TX, 77555-0609, USA
SOURCE: Trends in Parasitology (2001), 17(6), 269-272

CODEN: TPRACT; ISSN: 1471-4922
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 23 refs. Malaria transmission-blocking strategies aimed at disrupting parasite-mosquito interactions have the potential to make important contributions to global malaria control. It has been suggested that **Plasmodium**-secreted **chitinase** plays a crucial role in allowing the ookinete to initiate its invasion of the mosquito midgut, which suggests that this enzyme is a candidate target for blocking malaria transmission. In this review, the authors discuss **Plasmodium chitinases** from the mol., biochem. and cell biol. viewpoints. Future directions of study could involve developing strategies for interrupting the function of **Plasmodium chitinases** within the mosquito midgut, including transmission-blocking drugs or vaccines, or the development of **chitinase**-inhibitor-producing transgenic mosquitoes.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:398915 CAPLUS
DOCUMENT NUMBER: 135:74333
TITLE: Disruption of **Plasmodium falciparum chitinase** markedly impairs parasite invasion of mosquito midgut
AUTHOR(S): Tsai, Yao-Lung; Hayward, Rhian E.; Langer, Rebecca C.; Fidock, David A.; Vinetz, Joseph M.
CORPORATE SOURCE: WHO Collaborating Center for Tropical Diseases, Department of Pathology, University of Texas Medical Branch, Galveston, TX, 77555-0609, USA
SOURCE: Infection and Immunity (2001), 69(6), 4048-4054
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To initiate invasion of the mosquito midgut, **Plasmodium** ookinetes secrete chitinolytic activity to penetrate the peritrophic matrix surrounding the blood meal. While ookinetes of the avian malaria parasite **Plasmodium** gallinaceum appear to secrete products of two **chitinase** genes, to date only one **chitinase** gene, PfCHT1, has been identified in the nearly completed **Plasmodium falciparum** strain 3D7 genome database. To test the hypothesis that the single identified **chitinase** of P. **falciparum** is necessary for ookinete invasion, the PfCHT1 gene was disrupted 39 bp upstream of the stop codon. PfCHT1-disrupted parasites had normal gametocytogenesis, exflagellation, and ookinete formation but were markedly impaired in their ability to form oocysts in Anopheles freeborni midguts. Confocal microscopy demonstrated that the truncated PfCHT1 protein was present in mutant ookinetes but that the concn. of mutant PfCHT1 within the apical end of the ookinetes was substantially reduced. These data suggest that full-length PfCHT1 is essential for intracellular trafficking and secretion and that the PfCHT1 gene product is necessary for ookinetes to invade the mosquito midgut.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:398914 CAPLUS
DOCUMENT NUMBER: 135:134584
TITLE: Knockout of the rodent malaria parasite **chitinase** PbCHT1 reduces infectivity to mosquitoes
AUTHOR(S): Dessens, Johannes T.; Mendoza, Jacqui; Claudianos, Charles; Vinetz, Joseph M.; Khater, Emad; Hassard, Stuart; Ranawaka, Gaya R.; Sinden, Robert E.
CORPORATE SOURCE: Department of Biology, Imperial College of Science, Technology, London, SW7 2AZ, UK
SOURCE: Infection and Immunity (2001), 69(6), 4041-4047
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During mosquito transmission, malaria ookinetes must cross a chitin-contg. structure known as the peritrophic matrix (PM), which surrounds the infected blood meal in the mosquito midgut. In turn, ookinetes produce multiple **chitinase** activities presumably aimed at disrupting this phys. barrier to allow ookinete invasion of the midgut epithelium. **Plasmodium chitinase** activities are demonstrated targets for human and avian malaria transmission blockade with the **chitinase** inhibitor allosamidin. Here, we identify and characterize the first **chitinase** gene of a rodent malaria parasite, **Plasmodium** berghei. We show that the gene, named PbCHT1, is a structural ortholog of PgCHT1 of the avian malaria parasite **Plasmodium** gallinaceum and a paralog of PfCHT1 of the human malaria parasite **Plasmodium falciparum**. Targeted disruption of PbCHT1 reduced parasite infectivity in Anopheles stephensi mosquitoes by up to 90%. Redns. in infectivity were also obsd. in ookinete feeds-an artificial situation where midgut invasion occurs before PM formation-suggesting that PbCHT1 plays a role other than PM disruption. PbCHT1 null mutants had no residual ookinete-derived **chitinase** activity in vitro, suggesting that P. berghei ookinetes express only one **chitinase** gene. Moreover, PbCHT1 activity appeared insensitive to allosamidin inhibition, an observation that raises questions about the use of allosamidin and components like it as potential malaria transmission-blocking drugs. Taken together, these findings suggest a fundamental divergence among rodent, avian, and human malaria parasite **chitinases**, with implications for the evolution of **Plasmodium**-mosquito interactions.

IT **352053-33-9**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; knockout of the rodent malaria parasite **chitinase** PbCHT1 reduces infectivity to mosquitoes)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:861835 CAPLUS
DOCUMENT NUMBER: 134:26949
TITLE: **Plasmodium** gene CHT1 **chitinases** and cDNAs and methods for preventing malaria transmission by mosquitoes
INVENTOR(S): Vinetz, Joseph M.
PATENT ASSIGNEE(S): Board of Regents of the University of Texas System, USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073488	A1	20001207	WO 2000-US14536	20000526

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-136508P P 19990528
US 2000-180051P P 20000203

AB The present invention is directed to isolated nucleic acid mols. encoding **Plasmodium** sp. **chitinases**. Expression vectors and host cells comprising the nucleic acid mols. are also provided, as well as methods for increasing or decreasing the expression of the **chitinase** in host cells. The invention further provides methods of screening a substance for the ability of the substance to modify **chitinase** function, and a method for isolating other **chitinase** mols. DNA oligomers capable of hybridizing to the nucleic acid mol. encoding the **chitinase** are provided, which can be used to detect **chitinase** in a sample. An isolated **Plasmodium** sp. **chitinase** is also provided. Antibodies specific for the **chitinase**, and fragments thereof, are provided, as are compns. comprising the **chitinase** and a compatible carrier. The subject invention further provides methods of preventing infection of mosquitoes by **Plasmodium** sp. and methods of preventing transmission of malaria. Thus, the cDNAs for gene CHT1 **chitinases** of P. **falciparum** and P. gallinaceum were cloned and sequenced. The P. gallinaceum enzyme is produced as a preproenzyme; the P. **falciparum** has only a signal sequence. P. gallinaceum produces a second **chitinase**, the product of a second gene provisionally called CHT2. The P. **falciparum** CHT1 **chitinase** appears to be an ortholog of the P. gallinaceum CHT2 **chitinase**. The substrate specificity and pH profiles of the enzymes were detd.

IT **254095-21-1, Chitinase (Plasmodium falciparum** gene CHT1 precursor) **278627-22-8**
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL

(Biological study); USES (Uses)
(nucleotide sequence; **plasmodium** gene CHT1 **chitinases** and cDNAs and methods for preventing malaria transmission by mosquitoes)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:776463 CAPLUS
DOCUMENT NUMBER: 134:53651
TITLE: Micronemal transport of **Plasmodium** ookinete **chitinases** to the electron-dense area of the apical complex for extracellular secretion
AUTHOR(S): Langer, Rebecca C.; Hayward, Rhian E.; Tsuboi, Takafumi; Tachibana, Mayumi; Torii, Motomi; Vinetz, Joseph M.
CORPORATE SOURCE: World Health Organization Collaborating Center for Tropical Diseases, Department of Pathology, University of Texas Medical Branch, Galveston, TX, 77555-0609, USA
SOURCE: Infection and Immunity (2000), 68(11), 6461-6465
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Plasmodium** ookinetes secrete **chitinases** to penetrate the acellular, chitin-contg. peritrophic matrix of the mosquito midgut en route to invasion of the epithelium. **Chitinases** are potentially targets that can be used to block malaria transmission. We demonstrate here that **chitinases** of **Plasmodium falciparum** and P. gallinaceum are concd. at the apical end of ookinetes. The **chitinase** PgCHT1 of P. gallinaceum is present within ookinete micronemes and subsequently becomes localized in the electron-dense area of the apical complex. These observations suggest a pathway by which ookinetes secrete proteins extracellularly.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:251045 CAPLUS
DOCUMENT NUMBER: 133:70645
TITLE: **Chitinases** of the avian malaria parasite **Plasmodium** gallinaceum, a class of enzymes necessary for parasite invasion of the mosquito midgut
AUTHOR(S): Vinetz, Joseph M.; Valenzuela, Jesus G.; Specht, Charles A.; Aravind, L.; Langer, Rebecca C.; Ribeiro, Jose M. C.; Kaslow, David C.
CORPORATE SOURCE: World Health Organization Collaborating Center for Tropical Diseases, Department of Pathology, The University of Texas Medical Branch, Galveston, TX, 77615, USA
SOURCE: Journal of Biological Chemistry (2000), 275(14), 10331-10341

CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **Plasmodium** ookinete produces chitinolytic activity that allows the parasite to penetrate the chitin-contg. peritrophic matrix surrounding the blood meal in the mosquito midgut. Since the peritrophic matrix is a phys. barrier that the parasite must cross to invade the mosquito, and the presence of allosamidin, a **chitinase** inhibitor, in a blood meal prevents the parasite from invading the midgut epithelium, **chitinases** (3.2.1.14) are potential targets of malaria parasite transmission-blocking interventions. We have purified a **chitinase** of the avian malaria parasite **Plasmodium** gallinaceum and cloned the gene, PgCHT1, encoding it. PgCHT1 encodes catalytic and substrate-binding sites characteristic of family 18 glycohydrolases. Expressed in Escherichia coli strain AD494 (DE3), recombinant PgCHT1 was found to hydrolyze polymeric chitin, native chitin oligosaccharides, and 4-methylumbelliferone derivs. of chitin oligosaccharides. Allosamidin inhibited recombinant PgCHT1 with an IC50 of 7 .mu.M and differentially inhibited two chromatog. separable P. gallinaceum ookinete-produced **chitinase** activities with IC50 values of 7 and 12 .mu.M, resp. These two **chitinase** activities also had different pH activity profiles. These data suggest that the P. gallinaceum ookinete uses products of more than one **chitinase** gene to initiate mosquito midgut invasion.

IT **278627-22-8 278627-23-9**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(amino acid sequence; cloning and sequences of **chitinases** of avian malaria parasite **Plasmodium** gallinaceum, class of enzymes necessary for parasite invasion of mosquito midgut)

IT **278627-20-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; cloning and sequences of **chitinases** of avian malaria parasite **Plasmodium** gallinaceum, class of enzymes necessary for parasite invasion of mosquito midgut)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:767999 CAPLUS
DOCUMENT NUMBER: 132:89991
TITLE: The **chitinase** PfCHT1 from the human malaria parasite **Plasmodium falciparum** lacks proenzyme and chitin-binding domains and displays unique substrate preferences
AUTHOR(S): Vinetz, Joseph M.; Dave, Sanat K.; Specht, Charles A.; Brameld, Kenneth A.; Xu, Bo; Hayward, Rhian; Fidock, David A.
CORPORATE SOURCE: WHO Center for Tropical Diseases, University of

Texas Medical Branch, Galveston, TX, 77555, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1999), 96(24), 14061-14066
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Within hours after the ingestion of a blood meal, the mosquito midgut epithelium synthesizes a chitinous sac, the peritrophic matrix. **Plasmodium** ookinetes traverse the peritrophic matrix while escaping the mosquito midgut. **Chitinases** (EC 3.2.1.14) are crit. for parasite invasion of the midgut: the presence of the **chitinase** inhibitor, allosamidin, in an infectious blood meal prevents oocyst development. A **chitinase** gene, PgCHT1, recently has been identified in the avian malaria parasite P. gallinaceum. We used the sequence of PgCHT1 to identify a P. **falciparum chitinase** gene, PfCHT1, in the P. **falciparum** genome database. PfCHT1 differs from PgCHT1 in that the P. **falciparum** gene lacks proenzyme and chitin-binding domains. PfCHT1 was expressed as an active recombinant enzyme in Escherichia coli. PfCHT1 shares with PgCHT1 a substrate preference unique to **Plasmodium chitinases**: the enzymes cleave tri- and tetramers of GlcNAc from penta- and hexameric oligomers and are unable to cleave smaller native chitin oligosaccharides. The pH activity profile of PfCHT1 and its IC50 (40 nM) to allosamidin are distinct from endochitinase activities secreted by P. gallinaceum ookinetes. Homol. modeling predicts that PgCHT1 has a novel pocket in the catalytic active site that PfCHT1 lacks, which may explain the differential sensitivity of PfCHT1 and PgCHT1 to allosamidin. PfCHT1 may be the ortholog of a second, as yet unidentified, **chitinase** gene of P. gallinaceum. These results may allow us to develop novel strategies of blocking human malaria transmission based on interfering with P. **falciparum chitinase**.

IT **254095-21-1**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; cloning and sequence of **chitinase** PfCHT1 from human malaria parasite **Plasmodium falciparum** lacking proenzyme and chitin-binding domains and displaying unique substrate preferences)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:702998 CAPLUS
DOCUMENT NUMBER: 130:77782
TITLE: **Plasmodium** gallinaceum: use of antiserums to degenerate synthetic peptides derived from the active site of protozoal **chitinases** to characterize an ookinete-specific **chitinase**
AUTHOR(S): Vinetz, Joseph M.; Kaslow, David C.
CORPORATE SOURCE: Malaria Vaccines Section, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, 20892-0425,

USA
SOURCE: Exp. Parasitol. (1998), 90(2), 199-202
CODEN: EXPAAA; ISSN: 0014-4894
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors hypothesized that the amino acid sequence of the active site of P. gallinaceum **chitinase** would be similar to the amino acid sequence of other protozoal, nematode, and higher bacterial **chitinases** and designed synthetic peptides based upon these sequences. Degenerate and nondegenerate synthetic peptides based upon the active sites of other protozoal **chitinases** generated antisera that detected a .apprx.50-kDa ookinete stage-specific protein. Antisera that recognized the E. hystolytica **chitinase** active-site immunoeluted a protein with **chitinase** activity from P. gallinaceum ookinete exts.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:576376 CAPLUS
DOCUMENT NUMBER: 125:271009
TITLE: Different effects of modulation of mosquito (Diptera:Culicidae) trypsin activity on the infectivity of two human malaria (Hemosporidia:Plasmodidae) parasites
AUTHOR(S): Ramasamy, Manthri S.; Kulasekera, Ranjith; Srikrishnaraj, K. Alagaratnam; Ramasamy, Ranjan
CORPORATE SOURCE: Division of Life Sciences, Institute of Fundamental Studies, Kandy, Sri Lanka
SOURCE: J. Med. Entomol. (1996), 33(5), 777-782
CODEN: JMENA6; ISSN: 0022-2585
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Trypsin prodn. in the malaria vector Anopheles tessellatus peaks at 12-21 h after a blood meal. The presence of leupeptin or soybean trypsin inhibitor in a blood meal delayed the onset of maximal trypsin activity. Trypsin inhibitors in an infective blood meal increased the infectivity of **Plasmodium** vivax and decreased infectivity of P. **falciparum** to A. tessellatus. The opposite effects of trypsin inhibitors on infectivity of the 2 malaria parasites were attributed to differences in the biol. of the parasites within the midgut of the vector, particularly the time of ookinete formation and the requirement for activation of a **chitinase**.

L2 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:129620 CAPLUS
DOCUMENT NUMBER: 124:173275
TITLE: Antibody-mediated inhibition of Aedes aegypti midgut trypsins blocks sporogonic development of **Plasmodium** gallinaceum
AUTHOR(S): Shahabuddin, Mohammed; Lemos, Francisco J. A.; Kaslow, David C.; Jacods-Lorena, Marcelo
CORPORATE SOURCE: Lab. Parasitic Diseases, National Institutes Allergy Infectious Diseases, Bethesda, MD,

20892-0425, USA
SOURCE: Infect. Immun. (1996), 64(3), 739-43
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The peritrophic matrix (PM) that forms around a blood meal is a potential barrier for **Plasmodium** development in mosquitoes. Previously, we have shown that to traverse the PM, **Plasmodium** ookinetes secrete a prochitinase and that an inhibitor of **chitinase** blocks further parasite development. Here we report that it is the mosquito trypsin that activates the **Plasmodium** prochitinase. Trypsin was identified as the **chitinase**-activating enzyme by two criteria: (i) trypsin activity and activating activity comigrated on one-dimensional gels, and (ii) activating activity and penetration of the PM by **Plasmodium** parasites were both hindered by trypsin-specific inhibitors. Subsequently, we examd. the effect of antitrypsin antibodies on the parasite life cycle. Antibodies prepd. against a recombinant blackfly trypsin effectively and specifically inhibited mosquito trypsin activity. Moreover, when incorporated into an infective blood meal, the antitrypsin antibodies blocked infectivity of Aedes aegypti mosquitoes by **Plasmodium** gallinaceum. This block of infectivity could be reversed by exogenously provided **chitinase**, strongly suggesting that the antibodies act by inhibiting prochitinase activation and not on the parasite itself. This work led to the identification of a mosquito antigen, i.e., midgut trypsin, as a novel target for blocking malaria transmission.
IT **122781-23-1**, Prochitinase
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(antibody-mediated inhibition of Aedes aegypti midgut trypsin blocks sporogonic development of **Plasmodium** gallinaceum)

L2 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:650690 CAPLUS
DOCUMENT NUMBER: 121:250690
TITLE: **Plasmodium**: parasite **chitinase** and its role in malaria transmission
AUTHOR(S): Shahabuddin, Mohammed; Kaslow, David C.
CORPORATE SOURCE: Laboratory of Malaria Research, National Institute of Allergy and Infectious Diseases, Bethesda, MD, 20892, USA
SOURCE: Exp. Parasitol. (1994), 79(1), 85-8
CODEN: EXPAAA; ISSN: 0014-4894
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 10 refs.

L2 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:405371 CAPLUS
DOCUMENT NUMBER: 119:5371
TITLE: Transmission-blocking activity of a **chitinase** inhibitor and activation of malarial parasite **chitinase** by mosquito protease
AUTHOR(S): Shahabuddin, Mohammed; Toyoshima, Tetsuhiko;

Aikawa, Masamichi; Kaslow, David C.
CORPORATE SOURCE: Lab. Malar. Res., Natl. Inst. Infect. Dis., Bethesda, MD, 20892, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1993), 90(9), 4266-70
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During development in the mosquito midgut, malarial parasites must transverse a chitin-contg. peritrophic matrix (PM) that forms around the food bolus. Previously, M. Huber et al. (1991) reported that the parasite secretes a protein with **chitinase** activity, and they suggested that parasite **chitinase** (EC 3.2.1.14) plays an important role in the parasite's egress from the blood meal. Allosamidin, a specific inhibitor of **chitinase**, completely blocked oocyte development in vivo and thus blocked malaria parasite transmission. Addn. of exogenous **chitinase** to the blood meal prevented the PM from forming and reversed the transmission-blocking activity of allosamidin. Using exogenous **chitinase**, the authors also found that the PM does not limit the no. of parasites that develop into oocysts, suggesting that the parasite produces sufficient quantities of **chitinase** to penetrate this potential barrier. In addn., treatment of parasite **chitinase** with a diisopropyl fluorophosphate-sensitive trypsinlike protease from the mosquito midgut or endoproteinase Lys-C increased its enzymic activity. These results suggest that the malaria parasite has evolved an intricate mechanism to adapt to the PM and the protease-rich environment of the mosquito midgut.

L2 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:203243 CAPLUS
DOCUMENT NUMBER: 114:203243
TITLE: Malaria parasite **chitinase** and penetration of the mosquito peritrophic membrane
AUTHOR(S): Huber, Marcel; Cabib, Enrico; Miller, Louis H.
CORPORATE SOURCE: Lab. Parasitic Dis., Natl. Inst. Allergy and Infect. Dis., Bethesda, MD, 20892, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1991), 88(7), 2807-10
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Malaria parasites (ookinetes) appear to digest the peritrophic membrane in the mosquito midgut during penetration. Previous studies demonstrated that lectins specific for N-acetylglucosamine bind to the peritrophic membrane and proposed that the membrane contains chitin. The present study shows that the peritrophic membrane is digested by Serratia marcescens **chitinase** (EC 3.2.1.14), leading to the release of N-acetylglucosamine and fragmentation of the membrane. The presence of a malaria parasite **chitinase** that digests 4-methylumbelliferyl chitotriose is also reported. The enzyme is not detectable until 15 h after zygote formation, the time required for maturation of the parasite from a zygote to an ookinete, the invasive form of the parasite. At 20 h, the enzyme begins to appear in the culture supernatant. The **chitinase** extd. from the parasite and found in the culture supernatant consists of a major band and 2 minor bands of activity on native PAGE. The presence of chitin in the peritrophic membrane,

the disruption of the peritrophic membrane during invasion, and the presence of **chitinase** in ookinetes suggest that the **chitinase** in ookinetes is used in the penetration of the peritrophic membrane.

L2 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:420270 CAPLUS
DOCUMENT NUMBER: 111:20270
TITLE: Use of **chitinase** to facilitate detection of protozoan, helminth and single copy genes in squashed whole mosquitoes
AUTHOR(S): Sim, Betty Kim Lee; Romans, Patricia; Harun, Syahrial
CORPORATE SOURCE: Dep. Immunol., Walter Reed Army Inst. Res., Washington, DC, 20307-5100, USA
SOURCE: Mol. Biochem. Parasitol. (1989), 34(2), 127-34
CODEN: MBIPDP; ISSN: 0166-6851
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The application of DNA probes to detect foreign DNA in whole arthropods has been limited by the inability of the probes to distinguish between small quantities of target DNA and the background signal generated by nonspecific hybridization of mosquito material. Treatment of nitrocellulose filters upon which mosquitoes have been squashed with **chitinase** and proteinase K eliminates nonspecific hybridization of DNA probes to mosquito components. This technique was used to detect a single larva of Brugia malayi, sporozoites of **Plasmodium falciparum** and **Plasmodium** berghei, and a single-copy gene in directly squashed vector mosquitoes. Use of this simple, rapid technique should facilitate the successful use of DNA probes in field studies.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 10:24:54 ON 29 MAR 2002)
L3 93 S L2
L4 66 S L3 AND (OOKINET? OR SECRET?(3A)ZYGOT?)
L5 22 DUP REM L4 (44 DUPLICATES REMOVED)

L5 ANSWER 1 OF 22 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002125338 IN-PROCESS
DOCUMENT NUMBER: 21843152 PubMed ID: 11854247
TITLE: Monoclonal antibody against the **Plasmodium falciparum chitinase**, PfCHT1, recognizes a malaria transmission-blocking epitope in **Plasmodium** gallinaceum **ookinetes** unrelated to the **chitinase** PgCHT1.
AUTHOR: Langer Rebecca C; Li Fengwu; Popov Vsevolod; Kurosky Alexander; Vinetz Joseph M
CORPORATE SOURCE: World Health Organization Collaborating Center for Tropical Diseases and Department of Pathology, University of Texas Medical Branch, Galveston, Texas 77555, USA.
CONTRACT NUMBER: CA 88137 (NCI)
KO2 AI50049 (NIAID)
R01 AI45999 (NIAID)
T32-AI10756 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (2002 Mar) 70 (3) 1581-90.

Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020226
Last Updated on STN: 20020226

AB To initiate invasion of the mosquito midgut, **Plasmodium ookinetes** secrete **chitinases** that are necessary to cross the chitin-containing peritrophic matrix en route to invading the epithelial cell surface. To investigate **chitinases** as potential immunological targets of blocking malaria parasite transmission to mosquitoes, a monoclonal antibody (MAb) was identified that neutralized the enzymatic activity of the sole **chitinase** of **Plasmodium falciparum**, PfCHT1, identified to date. This MAb, designated 1C3, previously shown to react with an apical structure of P. **falciparum ookinetes**, also reacts with a discrete apical structure of P. gallinaceum **ookinetes**. In membrane feeding assays, MAb 1C3 markedly inhibited P. gallinaceum oocyst development in mosquito midguts. MAb 1C3 affinity isolated an approximately 210-kDa antigen which, under reducing conditions, became a 35-kDa antigen. This isolated 35-kDa protein cross-reacted with an antiserum raised against a synthetic peptide derived from the P. gallinaceum **chitinase** active site, PgCHT1, even though MAb 1C3 did not recognize native or recombinant PgCHT1 on Western blot. Therefore, this affinity-purified 35-kDa antigen appears similar to a previously identified protein, PgCHT2, a putative second **chitinase** of P. gallinaceum. Epitope mapping indicated MAb 1C3 recognized a region of PfCHT1 that diverges from a homologous amino acid sequence conserved within sequenced **chitinases** of P. berghei, P. yoelii, and P. gallinaceum (PgCHT1). A synthetic peptide derived from the mapped 1C3 epitope may be useful as a component of a subunit transmission-blocking vaccine.

L5 ANSWER 2 OF 22 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001699931 MEDLINE
DOCUMENT NUMBER: 21614910 PubMed ID: 11748169
TITLE: Identification of novel **Plasmodium** gallinaceum zygote- and **ookinete**-expressed proteins as targets for blocking malaria transmission.
AUTHOR: Langer Rebecca C; Li Fengwu; Vinetz Joseph M
CORPORATE SOURCE: WHO Collaborating Center for Tropical Disease, Department of Pathology, University of Texas Medical Branch, Galveston, Texas 77555, USA.
CONTRACT NUMBER: KO2 AI50049 (NIAID)
RO1 AI45999 (NIAID)
T32-AI07536 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (2002 Jan) 70 (1) 102-6.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011219
Last Updated on STN: 20020125

Entered Medline: 20020114

AB The development of transmission-blocking vaccines is one approach to malaria control. To identify novel **Plasmodium zygote-** and **ookinete-secreted** proteins as targets of blocking malaria transmission, monoclonal antibodies (MAbs) were produced against parasite-secreted proteins found in **Plasmodium** gallinaceum **ookinete** culture supernatants. Four MAbs-1A6, 2A5, 2B5, and 4B6-were identified that bound to P. gallinaceum zygotes and **ookinetes** in diverse patterns in terms of spatial localization on parasites, time course of antigen expression, and Western immunoblot patterns. MAbs 2A5 and 4B6 recognized more than one protein band as detected by Western immunoblot of P. gallinaceum **ookinete** supernatants. Beginning at 0 h postfertilization, MAb 2A5 recognized a diverse set of antigens; at 10 h postfertilization, MAb 4B6 recognized several antigens as well. MAb 1A6 recognized a single approximately 17-kDa protein, and 2B5 recognized a single approximately 32-kDa protein at 15 h postfertilization. In membrane feeding assays to assess the effect of these MAbs on P. gallinaceum infectivity for Aedes aegypti mosquitoes, the addition of MAbs 1A6 and 2B5 to infectious blood meals significantly inhibited oocyst development in the mosquito midgut. In contrast, MAb 2A5 seemed to enhance infectivity. These results demonstrate that **Plasmodium ookinetes** secrete proteins (in addition to previously characterized **chitinases**) that may be targets for blocking malaria transmission. Future investigation of **ookinete**-secreted neutralization-sensitive molecules should provide valuable insight into mechanisms by which **ookinetes** exit the blood meal, penetrate and transverse the peritrophic matrix, and invade the mosquito midgut epithelium.

L5 ANSWER 3 OF 22 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001371369 MEDLINE
DOCUMENT NUMBER: 21246712 PubMed ID: 11349075
TITLE: Disruption of **Plasmodium falciparum chitinase** markedly impairs parasite invasion of mosquito midgut.
AUTHOR: Tsai Y L; Hayward R E; Langer R C; Fidock D A; Vinetz J M
CORPORATE SOURCE: WHO Collaborating Center for Tropical Diseases, Department of Pathology, University of Texas Medical Branch, Galveston 77555-0609, USA.
CONTRACT NUMBER: RO1-AI 45999 (NIAID)
T32-AI07536 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (2001 Jun) 69 (6) 4048-54.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

AB To initiate invasion of the mosquito midgut, **Plasmodium ookinetes** secrete chitinolytic activity to penetrate the peritrophic matrix surrounding the blood meal. While **ookinetes** of the avian malaria parasite **Plasmodium**

gallinaceum appear to secrete products of two **chitinase** genes, to date only one **chitinase** gene, PfCHT1, has been identified in the nearly completed **Plasmodium falciparum** strain 3D7 genome database. To test the hypothesis that the single identified **chitinase** of P. **falciparum** is necessary for **ookinete** invasion, the PfCHT1 gene was disrupted 39 bp upstream of the stop codon. PfCHT1-disrupted parasites had normal gametocytogenesis, exflagellation, and **ookinete** formation but were markedly impaired in their ability to form oocysts in Anopheles freeborni midguts. Confocal microscopy demonstrated that the truncated PfCHT1 protein was present in mutant **ookinetes** but that the concentration of mutant PfCHT1 within the apical end of the **ookinetes** was substantially reduced. These data suggest that full-length PfCHT1 is essential for intracellular trafficking and secretion and that the PfCHT1 gene product is necessary for **ookinetes** to invade the mosquito midgut.

L5 ANSWER 4 OF 22 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001371368 MEDLINE
DOCUMENT NUMBER: 21246711 PubMed ID: 11349074
TITLE: Knockout of the rodent malaria parasite **chitinase** pbCHT1 reduces infectivity to mosquitoes.
AUTHOR: Dessens J T; Mendoza J; Claudianos C; Vinetz J M; Khater E; Hassard S; Ranawaka G R; Sinden R E
CORPORATE SOURCE: Department of Biology, Imperial College of Science, Technology, and Medicine, London SW7 2AZ, United Kingdom.. j.dessens@ic.ac.uk
SOURCE: INFECTION AND IMMUNITY, (2001 Jun) 69 (6) 4041-7. Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ305256
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

AB During mosquito transmission, malaria **ookinetes** must cross a chitin-containing structure known as the peritrophic matrix (PM), which surrounds the infected blood meal in the mosquito midgut. In turn, **ookinetes** produce multiple **chitinase** activities presumably aimed at disrupting this physical barrier to allow **ookinete** invasion of the midgut epithelium. **Plasmodium chitinase** activities are demonstrated targets for human and avian malaria transmission blockade with the **chitinase** inhibitor allosamidin. Here, we identify and characterize the first **chitinase** gene of a rodent malaria parasite, **Plasmodium** berghei. We show that the gene, named PbCHT1, is a structural ortholog of PgCHT1 of the avian malaria parasite **Plasmodium** gallinaceum and a paralog of PfCHT1 of the human malaria parasite **Plasmodium falciparum** . Targeted disruption of PbCHT1 reduced parasite infectivity in Anopheles stephensi mosquitoes by up to 90%. Reductions in infectivity were also observed in **ookinete** feeds-an artificial situation where midgut invasion occurs before PM

formation-suggesting that PbCHT1 plays a role other than PM disruption. PbCHT1 null mutants had no residual **ookinete**-derived **chitinase** activity in vitro, suggesting that P. berghei **ookinetes** express only one **chitinase** gene. Moreover, PbCHT1 activity appeared insensitive to allosamidin inhibition, an observation that raises questions about the use of allosamidin and components like it as potential malaria transmission-blocking drugs. Taken together, these findings suggest a fundamental divergence among rodent, avian, and human malaria parasite **chitinases**, with implications for the evolution of **Plasmodium**-mosquito interactions.

L5 ANSWER 5 OF 22 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001298281 MEDLINE
DOCUMENT NUMBER: 21273639 PubMed ID: 11378031
TITLE: **Plasmodium ookinete**-secreted **chitinase** and parasite penetration of the mosquito peritrophic matrix.
AUTHOR: Langer R C; Vinetz J M
CORPORATE SOURCE: WHO Collaborating Center for Tropical Diseases, University of Texas Medical Branch, Keiller 2.138, 301 University Blvd, Galveston, TX 77555-0609, USA.
SOURCE: Trends Parasitol, (2001 Jun) 17 (6) 269-72. Ref: 23
Journal code: DZF; 100966034. ISSN: 1471-4922.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010730
Last Updated on STN: 20010730
Entered Medline: 20010726

AB Malaria transmission-blocking strategies aimed at disrupting parasite-mosquito interactions have the potential to make important contributions to global malaria control. It has been suggested that **Plasmodium**-secreted **chitinase** plays a crucial role in allowing the **ookinete** to initiate its invasion of the mosquito midgut, which suggests that this enzyme is a candidate target for blocking malaria transmission. In this review, the authors discuss **Plasmodium chitinases** from the molecular, biochemical and cell biology viewpoints. Future directions of study could involve developing strategies for interrupting the function of **Plasmodium chitinases** within the mosquito midgut, including transmission-blocking drugs or vaccines, or the development of **chitinase**-inhibitor-producing transgenic mosquitoes.

L5 ANSWER 6 OF 22 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2000209408 MEDLINE
DOCUMENT NUMBER: 20209408 PubMed ID: 10744721
TITLE: **Chitinases** of the avian malaria parasite **Plasmodium** gallinaceum, a class of enzymes necessary for parasite invasion of the mosquito midgut.
AUTHOR: Vinetz J M; Valenzuela J G; Specht C A; Aravind L; Langer R C; Ribeiro J M; Kaslow D C

CORPORATE SOURCE: World Health Organization Collaborating Center for Tropical Diseases, Department of Pathology, the University of Texas Medical Branch, Galveston, Texas 77615, USA.. jovinetz@utmb.edu
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Apr 7) 275 (14) 10331-41.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF064079; GENBANK-AF072442
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000508

AB The **Plasmodium ookinete** produces chitinolytic activity that allows the parasite to penetrate the chitin-containing peritrophic matrix surrounding the blood meal in the mosquito midgut. Since the peritrophic matrix is a physical barrier that the parasite must cross to invade the mosquito, and the presence of allosamidin, a **chitinase** inhibitor, in a blood meal prevents the parasite from invading the midgut epithelium, **chitinases** (3.2.1.14) are potential targets of malaria parasite transmission-blocking interventions. We have purified a **chitinase** of the avian malaria parasite **Plasmodium** gallinaceum and cloned the gene, PgCHT1, encoding it. PgCHT1 encodes catalytic and substrate-binding sites characteristic of family 18 glycohydrolases. Expressed in Escherichia coli strain AD494 (DE3), recombinant PgCHT1 was found to hydrolyze polymeric chitin, native chitin oligosaccharides, and 4-methylumbelliferone derivatives of chitin oligosaccharides. Allosamidin inhibited recombinant PgCHT1 with an IC(50) of 7 microM and differentially inhibited two chromatographically separable P. gallinaceum **ookinete** -produced **chitinase** activities with IC(50) values of 7 and 12 microM, respectively. These two **chitinase** activities also had different pH activity profiles. These data suggest that the P. gallinaceum **ookinete** uses products of more than one **chitinase** gene to initiate mosquito midgut invasion.

L5 ANSWER 7 OF 22 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2001027234 MEDLINE
DOCUMENT NUMBER: 20490584 PubMed ID: 11035760
TITLE: Micronemal transport of **Plasmodium ookinete chitinases** to the electron-dense area of the apical complex for extracellular secretion.
AUTHOR: Langer R C; Hayward R E; Tsuboi T; Tachibana M; Torii M; Vinetz J M
CORPORATE SOURCE: World Health Organization Collaborating Center for Tropical Diseases, Department of Pathology, University of Texas Medical Branch, Galveston, Texas 77555-0609, USA.
CONTRACT NUMBER: RO1-AI 45999 (NIAID)
T32-AI07536 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (2000 Nov) 68 (11) 6461-5.
Journal code: GO7. ISSN: 0019-9567.
PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001115

AB **Plasmodium ookinetes** secrete **chitinases** to penetrate the acellular, chitin-containing peritrophic matrix of the mosquito midgut en route to invasion of the epithelium. **Chitinases** are potentially targets that can be used to block malaria transmission. We demonstrate here that **chitinases** of **Plasmodium falciparum** and P. gallinaceum are concentrated at the apical end of **ookinetes**. The **chitinase** PgCHT1 of P. gallinaceum is present within **ookinete** micronemes and subsequently becomes localized in the electron-dense area of the apical complex. These observations suggest a pathway by which **ookinetes** secrete proteins extracellularly.

L5 ANSWER 8 OF 22 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 2000233870 MEDLINE
DOCUMENT NUMBER: 20233870 PubMed ID: 10769222
TITLE: A tubular network associated with the brush-border surface of the Aedes aegypti midgut: implications for pathogen transmission by mosquitoes.
AUTHOR: Zieler H; Garon C F; Fischer E R; Shahabuddin M
CORPORATE SOURCE: Medical Entomology Section, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892-0425, USA.
SOURCE: JOURNAL OF EXPERIMENTAL BIOLOGY, (2000 May) 203 Pt 10 1599-611.
Journal code: I2F; 0243705. ISSN: 0022-0949.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000714
Last Updated on STN: 20000714
Entered Medline: 20000706

AB The mosquito Aedes aegypti is capable of transmitting a variety of pathogens to man and to other vertebrates. The midgut of this insect has been well-studied both as the tissue where the first contact occurs between ingested pathogens and the insect host, and as a model system for blood meal digestion in blood-sucking insects. To understand better the nature of the midgut surface encountered by parasites or viruses, we used scanning electron microscopy to identify the most prominent structures and cell morphologies on the luminal midgut surface. The luminal side of the midgut is a complex and layered set of structures. The microvilli that are found on most, but not all, cells are covered by a network of fine strands that we have termed the microvilli-associated network (MN). The MN strands are membranous, as shown by a membrane bilayer visible in cross sections of MN strands at high magnification in transmission electron micrographs. The MN is found in blood-fed as well as unfed mosquitoes and is not affected by **chitinase** treatment,

suggesting that it is not related to the chitinous peritrophic membrane that is formed only after blood feeding. The cells in the midgut epithelium have two distinct morphologies: the predominant cell type is densely covered with microvilli, while cells with fewer microvilli are found interspersed throughout the midgut. We used lectins to probe for the presence of carbohydrates on the midgut surface. A large number of lectins bind to the luminal midgut surface, suggesting that a variety of sugar linkages are present on the structures visualized by electron microscopy. Some of these lectins partially block attachment of malaria **ookinetes** to the midgut surface in vitro. Thus, the mosquito midgut epithelium, like the lining of mammalian intestines, is complex, composed of a variety of cell types and extensively covered with surface carbohydrate that may play a role in pathogen attachment.

L5 ANSWER 9 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:17983 BIOSIS
DOCUMENT NUMBER: PREV200100017983
TITLE: Identification of a novel secretory structure in **Plasmodium ookinetes** by a monoclonal antibody that recognizes a neutralization-sensitive epitope of **Plasmodium chitinases.**
AUTHOR(S): Langer, R. C. (1); Vinetz, J. M. (1)
CORPORATE SOURCE: (1) WHO Center for Tropical Diseases, University of Texas Medical Branch, Galveston, TX USA
SOURCE: American Journal of Tropical Medicine and Hygiene, (March, 2000) Vol. 62, No. 3 Supplement, pp. 205-206. print.
Meeting Info.: 49th Annual Meeting of the American Society of Tropical Medicine and Hygiene Houston, Texas, USA October 29-November 02, 2000 American Society of Tropical Medicine and Hygiene
. ISSN: 0002-9637.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L5 ANSWER 10 OF 22 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 2000040676 MEDLINE
DOCUMENT NUMBER: 20040676 PubMed ID: 10570198
TITLE: The **chitinase** PfCHT1 from the human malaria parasite **Plasmodium falciparum** lacks proenzyme and chitin-binding domains and displays unique substrate preferences.
AUTHOR: Vinetz J M; Dave S K; Specht C A; Brameld K A; Xu B; Hayward R; Fidock D A
CORPORATE SOURCE: WHO Center for Tropical Diseases, University of Texas Medical Branch, Galveston, TX 77555, USA.. jovinetz@utmb.edu
CONTRACT NUMBER: F32 AI-10416 (NIAID)
GM31318 (NIGMS)
GM54380 (NIGMS)
+
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Nov 23) 96 (24) 14061-6.
Journal code: PV3; 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF172445
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000106

AB Within hours after the ingestion of a blood meal, the mosquito midgut epithelium synthesizes a chitinous sac, the peritrophic matrix. **Plasmodium ookinetes** traverse the peritrophic matrix while escaping the mosquito midgut. **Chitinases** (EC 3.2.1.14) are critical for parasite invasion of the midgut: the presence of the **chitinase** inhibitor, allosamidin, in an infectious blood meal prevents oocyst development. A **chitinase** gene, PgCHT1, recently has been identified in the avian malaria parasite P. gallinaceum. We used the sequence of PgCHT1 to identify a P. **falciparum** **chitinase** gene, PfCHT1, in the P. **falciparum** genome database. PfCHT1 differs from PgCHT1 in that the P. **falciparum** gene lacks proenzyme and chitin-binding domains. PfCHT1 was expressed as an active recombinant enzyme in Escherichia coli. PfCHT1 shares with PgCHT1 a substrate preference unique to **Plasmodium chitinases**: the enzymes cleave tri- and tetramers of GlcNAc from penta- and hexameric oligomers and are unable to cleave smaller native chitin oligosaccharides. The pH activity profile of PfCHT1 and its IC(50) (40 nM) to allosamidin are distinct from endochitinase activities secreted by P. gallinaceum **ookinetes**. Homology modeling predicts that PgCHT1 has a novel pocket in the catalytic active site that PfCHT1 lacks, which may explain the differential sensitivity of PfCHT1 and PgCHT1 to allosamidin. PfCHT1 may be the ortholog of a second, as yet unidentified, **chitinase** gene of P. gallinaceum. These results may allow us to develop novel strategies of blocking human malaria transmission based on interfering with P. **falciparum** **chitinase**.

L5 ANSWER 11 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1999:59837 SCISEARCH
THE GENUINE ARTICLE: 154TL
TITLE: Mosquito - **Plasmodium** interactions in response to immune activation of the vector
AUTHOR: Lowenberger C A (Reprint); Kamal S; Chiles J; Paskewitz S; Bulet P; Hoffmann J A; Christensen B M
CORPORATE SOURCE: UNIV WISCONSIN, DEPT ENTOMOL, 1655 LINDEN DR, MADISON, WI 53706 (Reprint); CNRS, INST BIOL MOL & CELLULAIRE, UPR 9022, F-67084 STRASBOURG, FRANCE
COUNTRY OF AUTHOR: USA; FRANCE
SOURCE: EXPERIMENTAL PARASITOLOGY, (JAN 1999) Vol. 91, No. 1, pp. 59-69.
Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 0014-4894.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 42

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB During the development of **Plasmodium** sp, within the mosquito midgut, the parasite undergoes a series of developmental changes. The elongated **ookinete** migrates through the layers of the midgut where it forms the oocyst under the basal lamina. We demonstrate here that if Aedes aegypti or Anopheles gambiae, normally susceptible to **Plasmodium** gallinaceum and P. berghei, respectively, are immune activated by the injection of bacteria into the hemocoel, and subsequently are fed on an infectious bloodmeal, there is a significant reduction in the prevalence and mean intensity of infection of oocysts on the midgut. Only those mosquitoes immune activated prior to, or immediately after, parasite ingestion exhibit this reduction in parasite development. Mosquitoes immune activated 2-5 days after bloodfeeding show no differences in parasite burdens compared with naive controls. Northern analyses reveal that transcriptional activity for mosquito defensins is not detected in the whole bodies of Ae. aegypti from 4 h to 10 days after ingesting I? gallinaceum, suggesting that parasite ingestion; passage from the food bolus through the midgut, oocyst formation, and subsequent release of sporozoites into the hemolymph do not induce the production of defensin. However, reverse transcriptase-PCR of RNA isolated solely from the midguts of Ae. aegypti indicates that transcription of mosquito defensins occurs in the midguts of naive mosquitoes and those ingesting an infectious or noninfectious bloodmeal. Bacteria-challenged Ae. aegypti showed high levels of mature defensin in the hemolymph that correlate with a lower prevalence and mean intensity of infection with oocysts. Because few oocysts were found on the midgut of immune-activated mosquitoes, the data suggest,that some factor, induced by bacterial challenge, kills the parasite at a preoocyst stage. (C) 1999 Academic Press.

L5 ANSWER 12 OF 22 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 1998443216 MEDLINE
DOCUMENT NUMBER: 98443216 PubMed ID: 9769251
TITLE: **Plasmodium** gallinaceum: use of antisera to degenerate synthetic peptides derived from the active site of protozoal **chitinases** to characterize an **ookinete**-specific **chitinase**.
AUTHOR: Vinetz J M; Kaslow D C
CORPORATE SOURCE: Malaria Vaccines Section, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, 20892-0425, USA.
SOURCE: EXPERIMENTAL PARASITOLOGY, (1998 Oct) 90 (2) 199-202. Journal code: EQP; 0370713. ISSN: 0014-4894.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 19981029
Entered Medline: 19981022

L5 ANSWER 13 OF 22 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 1998360226 MEDLINE

DOCUMENT NUMBER: 98360226 PubMed ID: 9695113
TITLE: **Plasmodium ookinete** development in the mosquito midgut: a case of reciprocal manipulation.
AUTHOR: Shahabuddin M
CORPORATE SOURCE: Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892-0425, USA.
SOURCE: PARASITOLOGY, (1998) 116 Suppl S83-93. Ref: 95
Journal code: OR0; 0401121. ISSN: 0031-1820.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980903
Last Updated on STN: 19980903
Entered Medline: 19980827

AB The **ookinete** is one of the most important stages of **Plasmodium** development in the mosquito. It is morphologically and biochemically distinct from the earlier sexual stages--gametocytes and zygote, and from the later stages--oocyst and sporozoites. Development to **ookinete** allows the parasite to escape from the tightly packed blood bolus, to cross the sturdy peritrophic matrix (PM), to be protected from the digestive environment of the midgut lumen, and to invade the gut epithelium. The success of each of these activities may depend on the degree of the biochemical and physical barriers in the mosquito (such as density of blood bolus, thickness of peritrophic matrix, proteolytic activities in the gut lumen etc.) and the ability of the **ookinete** to overcome these barriers. **Ookinete** motility, secretion of **chitinase**, resistance to the digestive enzymes, and recognition/invasion of the midgut epithelium all may play crucial roles in the transformation to oocyst. The overall sporogonic development of **Plasmodium**, therefore, depends on the results of the two-way manipulations between the parasite and the vector mosquito. Study of **ookinete** development and of the cellular and biochemical complexities of the mosquito gut may therefore lead to the design of novel strategies to block the transmission of malaria. This article reviews the intricate interactions between the parasite and the mosquito midgut in the context of development and transmission of **Plasmodium** parasites.

L5 ANSWER 14 OF 22 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 97471321 MEDLINE
DOCUMENT NUMBER: 97471321 PubMed ID: 9330262
TITLE: Interactions of human malaria parasites, **Plasmodium** vivax and P.**falciparum**, with the midgut of Anopheles mosquitoes.
AUTHOR: Ramasamy M S; Kulasekera R; Wanniarachchi I C; Srikrishnaraj K A; Ramasamy R
CORPORATE SOURCE: Division of Life Sciences, Institute of Fundamental Studies, Kandy, Sri Lanka.
SOURCE: MEDICAL AND VETERINARY ENTOMOLOGY, (1997 Jul) 11 (3)

290-6. Ref: 70
Journal code: A9O; 8708682. ISSN: 0269-283X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971114

AB Present understanding of the development of sexual stages of the human malaria parasites **Plasmodium** vivax and P. **falciparum** in the Anopheles vector is reviewed, with particular reference to the role of the mosquito midgut in establishing an infection. The sexual stages of the parasite, the gametocytes, are formed in human erythrocytes. The changes in temperature and pH encountered by the gametocyte induce gametogenesis in the lumen of the midgut. Macromolecules derived from mosquito tissue and second messenger pathways regulate events leading to fertilization. In An.tessellatus the movement of the **ookinete** from the lumen to the midgut epithelium is linked to the release of trypsin in the midgut and the peritrophic matrix is not a firm barrier to this movement. The passage of the P.vivax **ookinete** through the peritrophic matrix may take place before the latter is fully formed. The late **ookinete** development in P.**falciparum** requires **chitinase** to facilitate penetration of the peritrophic matrix. Recognition sites for the **ookinetes** are present on the midgut epithelial cells. N-acetyl glucosamine residues in the oligosaccharide side chains of An.tessellatus midgut glycoproteins and peritrophic matrix proteoglycan may function as recognition sites for P.vivax and P.**falciparum ookinetes**. It is possible that **ookinetes** penetrating epithelial cells produce stress in the vector. Mosquito molecules may be involved in oocyst development in the basal lamina, and encapsulation of the parasite occurs in vectors that are refractory to the parasite. Detailed knowledge of vector-parasite interactions, particularly in the midgut and the identification of critical mosquito molecules offers prospects for manipulating the vector for the control of malaria.

L5 ANSWER 15 OF 22 SCISEARCH COPYRIGHT 2002 ISI (R)

ACCESSION NUMBER: 97:236457 SCISEARCH
THE GENUINE ARTICLE: WN333
TITLE: Transmission-blocking vaccines: Uses and current status of development
AUTHOR: Kaslow D C (Reprint)
CORPORATE SOURCE: NIAID, PARASIT DIS LAB, MALARIA VACCINES SECT, NIH, BETHESDA, MD 20892 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: INTERNATIONAL JOURNAL FOR PARASITOLOGY, (FEB 1997) Vol. 27, No. 2, pp. 183-189.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB.
ISSN: 0020-7519.

DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; AGRI
LANGUAGE: English
REFERENCE COUNT: 44
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Malaria continues to cause incomprehensible human suffering throughout most of the tropics and subtropics: in sub-Saharan Africa it is estimated that 2 million children die each year as a direct cause of infection with **Plasmodium**. Vector control and malaria chemotherapy that were previously effective in controlling and treating malaria are now largely ineffective due to insecticide-resistant mosquitoes and drug-resistant parasites. As alternatives to these mainstays of control, an intensive effort to develop subunit vaccines targeted at various stages of the life has been undertaken. One such vaccine, directed against the sexual and sporogonic stages and referred to as a transmission-blocking vaccine, offers the hope of controlling malaria in geographically isolated areas, preventing re-introduction of the parasite in malaria-free zones, blocking the spread of drug-resistant or vaccine escape mutants, and reducing exposure to ''virulent'' strains of parasites. A series of potential transmission-blocking vaccine candidates have identified and the genes encoding these surface proteins have now been isolated and sequenced. One such vaccine candidate, Pfs25, is now being tested in human Phase I safety and immunogenicity studies. Here the use and status of transmission-blocking vaccines are reviewed. Published by Elsevier Science Ltd.

L5 ANSWER 16 OF 22 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 96438252 MEDLINE
DOCUMENT NUMBER: 96438252 PubMed ID: 8840684
TITLE: Different effects of modulation of mosquito (Diptera:Culicidae) trypsin activity on the infectivity of two human malaria (Hemosporidia:Plasmodidae) parasites.
AUTHOR: Ramasamy M S; Kulasekera R; Srikrishnaraj K A; Ramasamy R
CORPORATE SOURCE: Division of Life Sciences, Institute of Fundamental Studies, Kandy, Sri Lanka.
SOURCE: JOURNAL OF MEDICAL ENTOMOLOGY, (1996 Sep) 33 (5) 777-82.
Journal code: J1B; 0375400. ISSN: 0022-2585.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961205

AB Trypsin production in the malaria vector Anopheles tessellatus Theobald peaks between 12 and 21 h after a blood meal. The presence of leupeptin or soybean trypsin inhibitor in a blood meal delayed the onset of maximal trypsin activity. Trypsin inhibitors in an infective blood meal increased the infectivity of **Plasmodium** vivax Grassi and decreased infectivity of P. **falciparum** Welch to An tessellatus. The opposite effects of trypsin inhibitors on infectivity of the 2 malaria parasites were attributed to

differences in the biology of the parasites within the midgut of the vector, particularly the time of **ookinete** formation and the requirement for activation of a **chitinase**.

L5 ANSWER 17 OF 22 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 96186467 MEDLINE
DOCUMENT NUMBER: 96186467 PubMed ID: 8641775
TITLE: Antibody-mediated inhibition of Aedes aegypti midgut trypsins blocks sporogonic development of **Plasmodium** gallinaceum.
AUTHOR: Shahabuddin M; Lemos F J; Kaslow D C; Jacobs-Lorena M
CORPORATE SOURCE: Laboratory of Parasitic Diseases, National Institutes of Allergy and Infectious Diseases, Bethesda, Maryland 20892-0425, USA.
SOURCE: INFECTION AND IMMUNITY, (1996 Mar) 64 (3) 739-43. Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960726
Last Updated on STN: 19960726
Entered Medline: 19960716

AB The peritrophic matrix (PM) that forms around a blood meal is a potential barrier of **Plasmodium** development in mosquitoes. Previously, we have shown that to traverse the PM, **Plasmodium ookinetes** secrete a prochitinase and that an inhibitor of **chitinase** blocks further parasite development. Here we report that it is the mosquito trypsin that activates the **Plasmodium** prochitinase. Trypsin was identified as the **chitinase**-activating enzyme by two criteria: (i) trypsin activity and activating activity comigrated on one-dimensional gels, and (ii) activating activity and penetration of the PM by **Plasmodium** parasites were both hindered by trypsin-specific inhibitors. Subsequently, we examined the effect of antitrypsin antibodies on the parasite life cycle. Antibodies prepared against a recombinant blackfly trypsin effectively and specifically inhibited mosquito trypsin activity. Moreover, when incorporated into an infective blood meal, the antitrypsin antibodies blocked infectivity of Aedes aegypti mosquitoes by **Plasmodium** gallinaceum. This block of infectivity could be reversed by exogenously provided **chitinase**, strongly suggesting that the antibodies act by inhibiting prochitinase activation and not on the parasite itself. This work led to the identification of a mosquito antigen, i.e., midgut trypsin, as a novel target for blocking malaria transmission.

L5 ANSWER 18 OF 22 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 95203403 MEDLINE
DOCUMENT NUMBER: 95203403 PubMed ID: 7534722
TITLE: Unique specificity of in vitro inhibition of mosquito midgut trypsin-like activity correlates with in vivo inhibition of malaria parasite infectivity.
AUTHOR: Shahabuddin M; Criscio M; Kaslow D C
CORPORATE SOURCE: Molecular Vaccine Section, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892.

SOURCE: EXPERIMENTAL PARASITOLOGY, (1995 Mar) 80 (2) 212-9.
Journal code: EQP; 0370713. ISSN: 0014-4894.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950504
Last Updated on STN: 19960129
Entered Medline: 19950421

AB Synchrony in the egress of **Plasmodium ookinetes** from the food bolus and enzymatic digestion of the blood meal in the mosquito midgut suggests that digestive enzymes play a role in the successful transmission of malaria parasites. Previously, we found that parasite-produced **chitinase** is essential for parasite transmission and can be activated by mosquito midgut protease. To determine the suitability of developing a transmission-blocking vaccine directed against mosquito trypsin-like enzyme(s), Aedes aegypti midgut trypsin-like proteases were characterized biochemically and compared to a mammalian trypsin. Mosquito trypsin is more sensitive to inhibition by aprotinin and less sensitive to egg white trypsin inhibitor than is bovine pancreatic trypsin. Soybean trypsin inhibitor and leupeptin inhibit both enzymes to similar extent. Membrane-feeding assays with aprotinin, leupeptin, and egg white trypsin inhibitor revealed a correlation between in vitro inhibition of mosquito trypsin-like activity and transmission-blocking activity. The results suggest a role for mosquito midgut trypsin(s) in malaria parasite development and indicate that the protease(s) is a potential target for blocking malaria transmission.

L5 ANSWER 19 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:62808 BIOSIS
DOCUMENT NUMBER: PREV199344028458
TITLE: **Chitinase**: A novel target for blocking transmission of malaria.
AUTHOR(S): Shahabuddin, M.; Keister, D. B.; Kaslow, D. C.
CORPORATE SOURCE: Lab. Malaria Res., National Inst. Allergy, Infectious Diseases, National Inst. Health, Bethesda, Md
SOURCE: American Journal of Tropical Medicine and Hygiene, (1992) Vol. 47, No. 4 SUPPL., pp. 260.
Meeting Info.: 41st Annual Meeting of the American Society of Tropical Medicine and Hygiene, Seattle, Washington, USA, November 15-19, 1992. AM J TROP MED HYG
ISSN: 0002-9637.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 20 OF 22 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 91187880 MEDLINE
DOCUMENT NUMBER: 91187880 PubMed ID: 2011589
TITLE: Malaria parasite **chitinase** and penetration of the mosquito peritrophic membrane.
AUTHOR: Huber M; Cabib E; Miller L H
CORPORATE SOURCE: Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892.

SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1991 Apr 1) 88 (7) 2807-10.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910526
Last Updated on STN: 19910526
Entered Medline: 19910506

AB Malaria parasites (**ookinetes**) appear to digest the peritrophic membrane in the mosquito midgut during penetration. Previous studies demonstrated that lectins specific for N-acetylglucosamine bind to the peritrophic membrane and proposed that the membrane contains chitin [Rudin, W. & Hecker, H. (1989) Parasitol. Res. 75, 268-279]. In the present study, we show that the peritrophic membrane is digested by Serratia marcescens **chitinase** (EC 3.2.1.14), leading to the release of N-acetylglucosamine and fragmentation of the membrane. We also report the presence of a malaria parasite **chitinase** that digests 4-methylumbelliferyl chitotriose. The enzyme is not detectable until 15 hr after zygote formation, the time required for maturation of the parasite from a zygote to an **ookinete**, the invasive form of the parasite. At 20 hr, the enzyme begins to appear in the culture supernatant. The **chitinase** extracted from the parasite and found in the culture supernatant consists of a major band and two minor bands of activity on native polyacrylamide gel electrophoresis. The presence of chitin in the peritrophic membrane, the disruption of the peritrophic membrane during invasion, and the presence of **chitinase** in **ookinetes** suggest that the **chitinase** in **ookinetes** is used in the penetration of the peritrophic membrane.

L5 ANSWER 21 OF 22 CONFSCI COPYRIGHT 2002 CSA

ACCESSION NUMBER: 2000:70541 CONFSCI
DOCUMENT NUMBER: 00-067412
TITLE: Identification of a novel secretory structure in **Plasmodium ookinetes** by a monoclonal antibody that recognizes a neutralization-sensitive epitope of **Plasmodium chitinases**
AUTHOR: Langer, R.C.; Vinetz, J.M.
CORPORATE SOURCE: WHO Cent. for Tropical Diseases, Univ. Texas Med. Branch, Galveston, TX, USA
SOURCE: American Society of Tropical Medicine and Hygiene, 3088 Briarcliff Rd., Ste. 11A, Atlanta, GA 30329, USA

Meeting Info.: 000 5172: ASTMH 49th Annual Meeting (0005172). Houston, Texas (USA). 29 Oct-2 Nov 2000. American Society of Tropical Medicine and Hygiene.
DOCUMENT TYPE: Conference
FILE SEGMENT: DCCP
LANGUAGE: English

L5 ANSWER 22 OF 22 CONFSCI COPYRIGHT 2002 CSA

ACCESSION NUMBER: 2000:70302 CONFSCI
DOCUMENT NUMBER: 00-067173
TITLE: Identification of a novel secretory structure in **Plasmodium ookinetes** by a monoclonal antibody that recognizes a neutralization-sensitive epitope of **Plasmodium chitinases**
AUTHOR: Langer, R.
SOURCE: American Society of Tropical Medicine and Hygiene, 3088 Briarcliff Rd., Ste. 11A, Atlanta, GA 30329, USA

Meeting Info.: 000 5172: ASTMH 49th Annual Meeting (0005172). Houston, Texas (USA). 29 Oct-2 Nov 2000. American Society of Tropical Medicine and Hygiene.
DOCUMENT TYPE: Conference
FILE SEGMENT: DCCP
LANGUAGE: English

FILE 'CAPLUS' ENTERED AT 10:29:35 ON 29 MAR 2002
L6 5 S (PF OR FALCIPAR?)(W)CHT# OR PFCHT#
L7 0 S L6 NOT L2

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 10:30:21 ON 29 MAR 2002
L8 16 S L6
L9 0 S L8 NOT L4

(FILE 'USPATFULL' ENTERED AT 10:31:04 ON 29 MAR 2002)
L10 9 S L2
L11 0 S L6

L10 ANSWER 1 OF 9 USPATFULL
ACCESSION NUMBER: 2001:178629 USPATFULL
TITLE: Human **chitinase**, its recombinant production, its use for decomposing chitin, its use in therapy or prophylaxis against infection diseases
INVENTOR(S): Aerts, Johannes Maria Franciscus Gerardus, Abcoude, Netherlands
PATENT ASSIGNEE(S): Universiteit Van Amsterdam, Amsterdm, Netherlands (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6303118	B1	20011016
APPLICATION INFO.:	US 1999-343623		19990630 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1995-486839, filed on 7 Jun 1995, now patented, Pat. No. US 5928928
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Prouty, Rebecca E.
LEGAL REPRESENTATIVE: Hoffman & Baron, LLP
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 1370
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A new human **chitinase** having an amino acid sequence as

shown in FIG. 1 or FIG. 2. Modified forms of it having a similar chitin-hydrolyzing activity, and antigenic peptides representing one of its epitopes. Recombinant production of the human **chitinase** by genetically engineered hosts or host cells. Recombinant nucleic acid encoding it, and human **chitinase** -specific oligonucleotides. Use for therapeutic or prophylactic treatment of humans against infection by chitin-containing pathogens, or for decomposing chitin, e.g. from chitin-based articles. Antibodies binding to the human **chitinase**. Diagnostic test kits comprising the human **chitinase**, its antigenic peptides, human **chitinase** antibodies, recombinant nucleic acid or oligonucleotides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/094.610
INCLS: 435/209.000; 536/023.200
NCL NCLM: 424/094.610
NCLS: 435/209.000; 536/023.200

L10 ANSWER 2 OF 9 USPATFULL

ACCESSION NUMBER:	2001:79288 USPATFULL
TITLE:	Genomic DNA sequences of ashbya gossypii and uses thereof
INVENTOR(S):	Philippsen, Peter, Riehen, Switzerland Pohlmann, Rainer, Lorrach, Germany, Federal Republic of Steiner-Lange, Sabine, Bonn, Germany, Federal Republic of Mohr, Christine, Allschwil, Switzerland Wendland, Jurgen, Lorrach, Germany, Federal Republic of Knechtle, Philipp, Oberwil, Switzerland Rebischung, Corinne, Saint-Louis, France
PATENT ASSIGNEE(S):	Syngenta Participations AG, Basel, Switzerland (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6239264	B1	20010529	
APPLICATION INFO.:	US 1997-998416		19971224	(8)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Priebe, Scott D.			
LEGAL REPRESENTATIVE:	Meigs, J. Timothy			
NUMBER OF CLAIMS:	2			
EXEMPLARY CLAIM:	1			
LINE COUNT:	4269			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the terminal sequencing of random genomic fragments performed with the filamentous fungus A.gossypii, to the sequences obtained therewith and the use of the sequences for forensic identification, to characterize genes and gene organization of this ascomycete by inter-genomic comparison, to identify biosynthetic genes that can be used as selection markers, to isolate promotors and terminators for application in a homologous as well as heterologous context, to find putative centromere containing clones, chromosome mapping, chromosome identifying, general information about chromosome organization and

in addition to identify ORF containing SRS sequences with no homology to S. cerevisiae or any other organism which allows the identification of A. gossypii specific genes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 536/023.100
INCLS: 435/320.100; 536/024.300; 536/024.320
NCL NCLM: 536/023.100
NCLS: 435/320.100; 536/024.300; 536/024.320

L10 ANSWER 3 OF 9 USPATFULL

ACCESSION NUMBER:	2001:25424 USPATFULL
TITLE:	Vectors for the diagnosis and treatment of solid tumors including melanoma
INVENTOR(S):	Pawelek, John M., Hamden, CT, United States Bermudes, David, Wallingford, CT, United States Low, Kenneth Brooks, Guilford, CT, United States
PATENT ASSIGNEE(S):	Yale University, New Haven, CT, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6190657	B1	20010220
APPLICATION INFO.:	US 1996-658034		19960604 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-486422, filed on 7 Jun 1995, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Ketter, James		
ASSISTANT EXAMINER:	Sandals, William		
LEGAL REPRESENTATIVE:	Pennie & Edmonds LLP		
NUMBER OF CLAIMS:	66		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	45 Drawing Figure(s); 38 Drawing Page(s)		
LINE COUNT:	4716		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to the isolation and use of super-infective, tumor-specific vectors that are strains of parasites including, but not limited to bacteria, fungi and protists. In certain embodiments the parasites include, but are not limited to, the bacterium Salmonella spp., such as Salmonella typhimurium, the bacterium Mycobacterium avium and the protozoan Leishmania amazonensis. In other embodiments, the present invention is concerned with the isolation of super-infective, tumor-specific, suicide gene-containing strains of parasites for use in treatment of solid tumors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/093.100
INCLS: 424/093.200; 424/282.100; 435/004.000; 435/069.100; 435/243.000; 435/252.300; 436/543.000; 536/023.100
NCL NCLM: 424/093.100
NCLS: 424/093.200; 424/282.100; 435/004.000; 435/069.100; 435/243.000; 435/252.300; 436/543.000; 536/023.100

L10 ANSWER 4 OF 9 USPATFULL
ACCESSION NUMBER: 2001:14468 USPATFULL
TITLE: Methods and compositions for targeting DNA

metabolic processes using aminoglycoside derivatives

INVENTOR(S): Hockensmith, Joel W., Charlottesville, VA, United States
Muthuswami, Rohini, Denver, CO, United States

PATENT ASSIGNEE(S): The University of Virginia Patent Foundation, Charolottesville, VA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6180612	B1	20010130
APPLICATION INFO.:	US 1998-179558		19981027 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1998-60470, filed on 15 Apr 1998, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-63898P	19971031 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Slobodyansky, Elizabeth
LEGAL REPRESENTATIVE: Pennie & Edmonds LLP
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 28 Drawing Figure(s); 23 Drawing Page(s)
LINE COUNT: 4170
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Protein targets for disease intervention through inhibition of nucleic acid metabolism are disclosed. Novel polypeptides for one such target, DNA-dependent ATPase A, and novel polynucleotides encoding DNA-dependent ATPase A are disclosed. Phosphoaminoglycoside compounds which act on such protein targets to inhibit nucleic acid metabolism. In addition, screening assays for identifying compounds that inhibit nucleic acid-dependent ATPase activity, including, but not limited to, DNA-dependent ATPase A, are disclosed. Such compounds are useful in the treatment of diseases, including but not limited to cancer and infectious disease, through disruption of nucleic acid metabolism and induction of apoptosis. Moreover, methods for prevention and treatment of diseases including, but not limited to cancer and infectious disease are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/025.000
INCLS: 514/039.000; 514/041.000
NCL NCLM: 514/025.000
NCLS: 514/039.000; 514/041.000

L10 ANSWER 5 OF 9 USPATFULL
ACCESSION NUMBER: 2001:8225 USPATFULL
TITLE: Development of a novel gene delivery system through seed coating
INVENTOR(S): Rush, Charles M., Amarillo, TX, United States
PATENT ASSIGNEE(S): Texas A & M University, College Station, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE

PATENT INFORMATION:	US 6175059	B1	20010116
APPLICATION INFO.:	US 1997-822124		19970321 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Hutzell, Paula K.
ASSISTANT EXAMINER: Zaghmout, Ousama M-Faiz
LEGAL REPRESENTATIVE: Fulbright & Jaworski, L.L.P.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1,7
LINE COUNT: 2692
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention describes a novel means of introducing foreign genes and/or viruses, wildtype or recombinant, into plant cells via a seed treatment method using recombinant or wildtype furoviruses and their natural fungal vectors. Because of its ease of application, longevity of the seed treatment product, minimal risk of transmission to subsequent seed generations, specificity, and universality within a species, it offers a significant improvement over prior art techniques for viral mediated gene delivery techniques. The unique and critical aspect of the invention is the use of seed treatment technology for delivering foreign genes or viruses into plants for, for example, the enhancement of agronomic traits and production of desirable products such as pharmaceuticals.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 800/279.000
INCLS: 800/278.000; 435/468.000; 435/254.110; 427/004.000; 424/093.000; 424/093.200; 424/093.210; 424/093.500
NCL NCLM: 800/279.000
NCLS: 424/093.200; 424/093.210; 424/093.500; 427/004.000; 435/254.110; 435/468.000; 800/278.000

L10 ANSWER 6 OF 9 USPATFULL
ACCESSION NUMBER: 2000:53926 USPATFULL
TITLE: Human **chitinase**, its recombinant production, its use for decomposing chitin, its use in therapy or prophylaxis against infection diseases
INVENTOR(S): Aerts, Johannes Maria Franciscus Gerardus, Abcoude, Netherlands
PATENT ASSIGNEE(S): Universiteit Van Amsterdam, Amsterdam, Netherlands (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6057142		20000502
APPLICATION INFO.:	US 1998-151011		19980910 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1995-486839, filed on 17 Jun 1995, now patented, Pat. No. US 5928928
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Prouty, Rebecca E.
LEGAL REPRESENTATIVE: Hoffmann & Baron, LLP
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)

LINE COUNT: 1655
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A new human **chitinase** having an amino acid sequence as shown in FIG. 1 or FIG. 2. Modified forms of it having a similar chitin-hydrolyzing activity, and antigenic peptides representing one of its epitopes. Recombinant production of the human **chitinase** by genetically engineered hosts or host cells. Recombinant nucleic acid encoding it, and human **chitinase** -specific oligonucleotides. Use for therapeutic or prophylactic treatment of humans against infection by chitin-containing pathogens, or for decomposing chitin, e.g. from chitin-based articles. Antibodies binding to the human **chitinase**. Diagnostic test kits comprising the human **chitinase**, its antigenic peptides, human **chitinase** antibodies, recombinant nucleic acid or oligonucleotides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/209.000
INCLS: 435/252.300; 435/325.000; 435/320.100; 536/023.200
NCL NCLM: 435/209.000
NCLS: 435/252.300; 435/320.100; 435/325.000; 536/023.200

L10 ANSWER 7 OF 9 USPATFULL
ACCESSION NUMBER: 1999:85279 USPATFULL
TITLE: Human **chitinase**, its recombinant production, its use for decomposing chitin, its use in therapy or prophylaxis against infection diseases
INVENTOR(S): Aerts, Johannes Maria Franciscus Gerardus, Abcoude, Netherlands
PATENT ASSIGNEE(S): Universiteit Van Amsterdam, Amsterdam, Netherlands (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5928928		19990727	
APPLICATION INFO.:	US 1995-486839		19950607	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Zitomer, Stephanie W.
ASSISTANT EXAMINER: Whisenant, Ethan
LEGAL REPRESENTATIVE: Hoffmann & Baron, LLP
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 1616
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A new human **chitinase** having an amino acid sequence as shown in FIG. 1 or FIG. 2. Modified forms of it having a similar chitin-hydrolyzing activity, and antigenic peptides representing one of its epitopes. Recombinant production of the human **chitinase** by genetically engineered hosts or host cells. Recombinant nucleic acid encoding it, and human **chitinase** -specific oligonucleotides. Use for therapeutic or prophylactic treatment of humans against infection by chitin-containing pathogens, or for decomposing chitin, e.g. from chitin-based articles. Antibodies binding to the human **chitinase**. Diagnostic test kits comprising the human chitanase, its antigenic

peptides, human **chitinase** antibodies, recombinant nucleic acid or oligonucleotides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/201.000
INCLS: 530/350.000; 435/183.000; 536/023.100; 536/024.300
NCL NCLM: 435/201.000
NCLS: 435/183.000; 530/350.000; 536/023.100; 536/024.300

L10 ANSWER 8 OF 9 USPATFULL

ACCESSION NUMBER:	91:66733 USPATFULL
TITLE:	Heliothis expression systems
INVENTOR(S):	Fraser, Malcolm J., South Bend, IN, United States Rosen, Elliot D., South Bend, IN, United States Ploplis, Victoria A., South Bend, IN, United States
PATENT ASSIGNEE(S):	American Biogenetic Science, Inc., Copiague, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5041379		19910820
APPLICATION INFO.:	US 1988-168109		19880314 (7)

RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1987-26499, filed on 16 Mar 1987, now abandoned
DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Schwartz, Richard A.
ASSISTANT EXAMINER:	Peet, Richard C.
LEGAL REPRESENTATIVE:	Pennie & Edmonds
NUMBER OF CLAIMS:	15
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	26 Drawing Figure(s); 25 Drawing Page(s)
LINE COUNT:	3494

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to recombinant vector/host systems which can direct the expression of foreign genes under the control of the Heliothis polyhedrin promoter. Using the systems of the present invention, a heterologous gene of interest can be expressed as an unfused peptide or protein, a fusion protein, or as a recombinant occlusion body which comprises crystallized polyhedrin fusion proteins bearing the heterologous gene product on the surface of or within the occlusion body. The recombinant proteins or occlusion bodies of the present invention have uses in vaccine formulations and immunoassays, as biological insecticides, and as expression systems for the production of foreign peptides or proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/235.100
INCLS: 435/069.100; 435/070.100; 435/091.000; 435/172.300; 435/240.200; 435/320.100; 536/027.000; 935/003.000; 935/006.000; 935/009.000; 935/022.000; 935/033.000; 935/034.000; 935/047.000; 935/048.000; 935/059.000; 935/060.000; 935/061.000; 935/066.000; 935/070.000
NCL NCLM: 435/235.100
NCLS: 435/069.100; 435/070.100; 435/320.100; 536/023.200; 536/023.600; 536/023.720

L10 ANSWER 9 OF 9 USPATFULL

ACCESSION NUMBER:	89:80739 USPATFULL
TITLE:	Recombinant baculovirus occlusion bodies in vaccines and biological insecticides
INVENTOR(S):	Fraser, Malcolm J., South Bend, IN, United States Rosen, Elliot D., South Bend, IN, United States Ploplis, Victoria A., South Bend, IN, United States
PATENT ASSIGNEE(S):	American Biogenetic Sciences, Inc., Copiague, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4870023		19890926
APPLICATION INFO.:	US 1988-153736		19880208 (7)

RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1987-26498, filed on 16 Mar 1987, now abandoned which is a continuation-in-part of Ser. No. US 1987-26499, filed on 16 Mar 1987
DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Wiseman, Thomas G.
ASSISTANT EXAMINER:	Seidman, Stephanie
LEGAL REPRESENTATIVE:	Pennie & Edmonds
NUMBER OF CLAIMS:	51
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	28 Drawing Figure(s); 26 Drawing Page(s)
LINE COUNT:	3868

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to recombinant baculoviruses which encode fusion polyhedrin proteins capable of forming occlusion bodies containing foreign peptides. The recombinant baculoviruses of the invention are formed by insertion into or replacement of regions of the polyhedrin gene that are not essential for occlusion body formation, with foreign DNA fragments by recombinant DNA techniques. The recombinant occlusion bodies produced in accordance with the present invention have uses in vaccine formulations, immunoassays, immobilized enzyme reactions, as biological insecticides, and as expression vectors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL	INCLM:	435/320.000
	INCLS:	435/068.000; 435/091.000; 435/172.300; 435/235.000; 435/243.000; 536/027.000; 935/032.000; 935/057.000; 935/070.000; 530/350.000; 530/820.000; 530/826.000
NCL	NCLM:	435/235.100
	NCLS:	435/069.300; 435/069.700; 435/243.000; 435/320.100; 530/350.000; 530/820.000; 530/826.000; 536/023.100; 536/023.400; 930/010.000; 930/220.000

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, ~~MICST-EPLUS~~, JAPIO, USPATFULL' ENTERED AT 10:33:02 ON 29 MAR 2002)

L12 51 S VINETZ J?/AU AND L2

L13 14 DUP REM L12 (37 DUPLICATES REMOVED)

- Author

L13 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1

ACCESSION NUMBER: 2002:150653 CAPLUS

TITLE: Monoclonal antibody against the **Plasmodium falciparum** **chitinase**, PfCHT1, recognizes a malaria transmission-blocking epitope in **Plasmodium** gallinaceum ookinetes unrelated to the **chitinase** PgCHT1

AUTHOR(S): Langer, Rebecca C.; Li, Fengwu; Popov, Vsevolod; Kurosky, Alexander; **Vinetz, Joseph M.**

CORPORATE SOURCE: World Health Organization Collaborating Center for Tropical Diseases, Department of Pathology, University of Texas Medical Branch, Galveston, TX, 77555, USA

SOURCE: Infection and Immunity (2002), 70(3), 1581-1590
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To initiate invasion of the mosquito midgut, **Plasmodium** ookinetes secrete **chitinases** that are necessary to cross the chitin-contg. peritrophic matrix en route to invading the epithelial cell surface. To investigate **chitinases** as potential immunol. targets of blocking malaria parasite transmission to mosquitoes, a monoclonal antibody (MAb) was identified that neutralized the enzymic activity of the sole **chitinase** of **Plasmodium falciparum**, PfCHT1, identified to date. This MAb, designated 1C3, previously shown to react with an apical structure of P. **falciparum** ookinetes, also reacts with a discrete apical structure of P. gallinaceum ookinetes. In membrane feeding assays, MAb 1C3 markedly inhibited P. gallinaceum oocyst development in mosquito midguts. MAb 1C3 affinity isolated an .apprx.210-kDa antigen which, under reducing conditions, became a 35-kDa antigen. This isolated 35-kDa protein cross-reacted with an antiserum raised against a synthetic peptide derived from the P. gallinaceum **chitinase** active site, PgCHT1, even though MAb 1C3 did not recognize native or recombinant PgCHT1 on Western blot. Therefore, this affinity-purified 35-kDa antigen appears similar to a previously identified protein, PgCHT2, a putative second **chitinase** of P. gallinaceum. Epitope mapping indicated MAb 1C3 recognized a region of PfCHT1 that diverges from a homologous amino acid sequence conserved within sequenced **chitinases** of P. berghei, P. yoelii, and P. gallinaceum (PgCHT1). A synthetic peptide derived from the mapped 1C3 epitope may be useful as a component of a subunit transmission-blocking vaccine.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2

ACCESSION NUMBER: 2001:936235 CAPLUS

DOCUMENT NUMBER: 136:198522

TITLE: Identification of novel **Plasmodium** gallinaceum zygote- and ookinete-expressed proteins as targets for blocking malaria transmission

AUTHOR(S): Langer, Rebecca C.; Li, Fengwu; **Vinetz, Joseph M.**

CORPORATE SOURCE: WHO Collaborating Center for Tropical Disease, Department of Pathology, University of Texas

Medical Branch, Galveston, TX, 77555, USA
SOURCE: Infection and Immunity (2002), 70(1), 102-106
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The development of transmission-blocking vaccines is one approach to malaria control. To identify novel **Plasmodium** zygote- and ookinete-secreted proteins as targets of blocking malaria transmission, monoclonal antibodies (MAbs) were produced against parasite-secreted proteins found in **Plasmodium** gallinaceum ookinete culture supernatants. Four MAbs-1A6, 2A5, 2B5, and 4B6-were identified that bound to P. gallinaceum zygotes and ookinetes in diverse patterns in terms of spatial localization on parasites, time course of antigen expression, and Western immunoblot patterns. MAbs 2A5 and 4B6 recognized more than one protein band as detected by Western immunoblot of P. gallinaceum ookinete supernatants. Beginning at 0 h postfertilization, MAb 2A5 recognized a diverse set of antigens; at 10 h postfertilization, MAb 4B6 recognized several antigens as well. MAb 1A6 recognized a single .apprx.17-kDa protein, and 2B5 recognized a single .apprx.32-kDa protein at 15 h postfertilization. In membrane feeding assays to assess the effect of these MAbs on P. gallinaceum infectivity for Aedes aegypti mosquitoes, the addn. of MAbs 1A6 and 2B5 to infectious blood meals significantly inhibited oocyst development in the mosquito midgut. In contrast, MAb 2A5 seemed to enhance infectivity. These results demonstrate that **Plasmodium** ookinetes secrete proteins (in addn. to previously characterized **chitinases**) that may be targets for blocking malaria transmission. Future investigation of ookinete-secreted neutralization-sensitive mols. should provide valuable insight into mechanisms by which ookinetes exit the blood meal, penetrate and transverse the peritrophic matrix, and invade the mosquito midgut epithelium.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2001:398915 CAPLUS
DOCUMENT NUMBER: 135:74333
TITLE: Disruption of **Plasmodium falciparum chitinase** markedly impairs parasite invasion of mosquito midgut
AUTHOR(S): Tsai, Yao-Lung; Hayward, Rhian E.; Langer, Rebecca C.; Fidock, David A.; **Vinetz, Joseph M.**
CORPORATE SOURCE: WHO Collaborating Center for Tropical Diseases, Department of Pathology, University of Texas Medical Branch, Galveston, TX, 77555-0609, USA
SOURCE: Infection and Immunity (2001), 69(6), 4048-4054
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To initiate invasion of the mosquito midgut, **Plasmodium** ookinetes secrete chitinolytic activity to penetrate the peritrophic matrix surrounding the blood meal. While ookinetes of the avian

malaria parasite **Plasmodium** gallinaceum appear to secrete products of two **chitinase** genes, to date only one **chitinase** gene, PfCHT1, has been identified in the nearly completed **Plasmodium falciparum** strain 3D7 genome database. To test the hypothesis that the single identified **chitinase** of P. **falciparum** is necessary for ookinete invasion, the PfCHT1 gene was disrupted 39 bp upstream of the stop codon. PfCHT1-disrupted parasites had normal gametocytogenesis, exflagellation, and ookinete formation but were markedly impaired in their ability to form oocysts in Anopheles freeborni midguts. Confocal microscopy demonstrated that the truncated PfCHT1 protein was present in mutant ookinetes but that the concn. of mutant PfCHT1 within the apical end of the ookinetes was substantially reduced. These data suggest that full-length PfCHT1 is essential for intracellular trafficking and secretion and that the PfCHT1 gene product is necessary for ookinetes to invade the mosquito midgut.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 2001:398914 CAPLUS
DOCUMENT NUMBER: 135:134584
TITLE: Knockout of the rodent malaria parasite **chitinase** PbCHT1 reduces infectivity to mosquitoes
AUTHOR(S): Dessens, Johannes T.; Mendoza, Jacqui; Claudianos, Charles; **Vinetz, Joseph M.**; Khater, Emad; Hassard, Stuart; Ranawaka, Gaya R.; Sinden, Robert E.
CORPORATE SOURCE: Department of Biology, Imperial College of Science, Technology, London, SW7 2AZ, UK
SOURCE: Infection and Immunity (2001), 69(6), 4041-4047
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During mosquito transmission, malaria ookinetes must cross a chitin-contg. structure known as the peritrophic matrix (PM), which surrounds the infected blood meal in the mosquito midgut. In turn, ookinetes produce multiple **chitinase** activities presumably aimed at disrupting this phys. barrier to allow ookinete invasion of the midgut epithelium. **Plasmodium chitinase** activities are demonstrated targets for human and avian malaria transmission blockade with the **chitinase** inhibitor allosamidin. Here, we identify and characterize the first **chitinase** gene of a rodent malaria parasite, **Plasmodium** berghei. We show that the gene, named PbCHT1, is a structural ortholog of PgCHT1 of the avian malaria parasite **Plasmodium** gallinaceum and a paralog of PfCHT1 of the human malaria parasite **Plasmodium falciparum**. Targeted disruption of PbCHT1 reduced parasite infectivity in Anopheles stephensi mosquitoes by up to 90%. Redns. in infectivity were also obsd. in ookinete feeds-an artificial situation where midgut invasion occurs before PM formation-suggesting that PbCHT1 plays a role other than PM disruption. PbCHT1 null mutants had no residual ookinete-derived **chitinase** activity in vitro,

suggesting that P. berghei ookinetes express only one **chitinase** gene. Moreover, PbCHT1 activity appeared insensitive to allosamidin inhibition, an observation that raises questions about the use of allosamidin and components like it as potential malaria transmission-blocking drugs. Taken together, these findings suggest a fundamental divergence among rodent, avian, and human malaria parasite **chitinases**, with implications for the evolution of **Plasmodium**-mosquito interactions.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
ACCESSION NUMBER: 2001:506637 CAPLUS
DOCUMENT NUMBER: 135:177745
TITLE: **Plasmodium** ookinete-secreted **chitinase** and parasite penetration of the mosquito peritrophic matrix
AUTHOR(S): Langer, Rebecca C.; **Vinetz, Joseph M.**
CORPORATE SOURCE: WHO Collaborating Center for Tropical Diseases, University of Texas Medical Branch, Galveston, TX, 77555-0609, USA
SOURCE: Trends in Parasitology (2001), 17(6), 269-272
CODEN: TPRACT; ISSN: 1471-4922
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 23 refs. Malaria transmission-blocking strategies aimed at disrupting parasite-mosquito interactions have the potential to make important contributions to global malaria control. It has been suggested that **Plasmodium**-secreted **chitinase** plays a crucial role in allowing the ookinete to initiate its invasion of the mosquito midgut, which suggests that this enzyme is a candidate target for blocking malaria transmission. In this review, the authors discuss **Plasmodium** **chitinases** from the mol., biochem. and cell biol. viewpoints. Future directions of study could involve developing strategies for interrupting the function of **Plasmodium** **chitinases** within the mosquito midgut, including transmission-blocking drugs or vaccines, or the development of **chitinase**-inhibitor-producing transgenic mosquitoes.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
ACCESSION NUMBER: 2000:861835 CAPLUS
DOCUMENT NUMBER: 134:26949
TITLE: **Plasmodium** gene CHT1 **chitinases** and cDNAs and methods for preventing malaria transmission by mosquitoes
INVENTOR(S): **Vinetz, Joseph M.**
PATENT ASSIGNEE(S): Board of Regents of the University of Texas System, USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073488	A1	20001207	WO 2000-US14536	20000526

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-136508P P 19990528
US 2000-180051P P 20000203

AB The present invention is directed to isolated nucleic acid mols. encoding **Plasmodium** sp. **chitinases**. Expression vectors and host cells comprising the nucleic acid mols. are also provided, as well as methods for increasing or decreasing the expression of the **chitinase** in host cells. The invention further provides methods of screening a substance for the ability of the substance to modify **chitinase** function, and a method for isolating other **chitinase** mols. DNA oligomers capable of hybridizing to the nucleic acid mol. encoding the **chitinase** are provided, which can be used to detect **chitinase** in a sample. An isolated **Plasmodium** sp. **chitinase** is also provided. Antibodies specific for the **chitinase**, and fragments thereof, are provided, as are compns. comprising the **chitinase** and a compatible carrier. The subject invention further provides methods of preventing infection of mosquitoes by **Plasmodium** sp. and methods of preventing transmission of malaria. Thus, the cDNAs for gene CHT1 **chitinases** of P. **falciparum** and P. gallinaceum were cloned and sequenced. The P. gallinaceum enzyme is produced as a preproenzyme; the P. **falciparum** has only a signal sequence. P. gallinaceum produces a second **chitinase**, the product of a second gene provisionally called CHT2. The P. **falciparum** CHT1 **chitinase** appears to be an ortholog of the P. gallinaceum CHT2 **chitinase**. The substrate specificity and pH profiles of the enzymes were detd.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 7
ACCESSION NUMBER: 2000:251045 CAPLUS
DOCUMENT NUMBER: 133:70645
TITLE: **Chitinases** of the avian malaria parasite **Plasmodium** gallinaceum, a class of enzymes necessary for parasite invasion of the mosquito midgut
AUTHOR(S): **Vinetz, Joseph M.**; Valenzuela, Jesus G.; Specht, Charles A.; Aravind, L.; Langer, Rebecca C.; Ribeiro, Jose M. C.; Kaslow, David C.
CORPORATE SOURCE: World Health Organization Collaborating Center

for Tropical Diseases, Department of Pathology, The University of Texas Medical Branch, Galveston, TX, 77615, USA
SOURCE: Journal of Biological Chemistry (2000), 275(14), 10331-10341
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **Plasmodium** ookinete produces chitinolytic activity that allows the parasite to penetrate the chitin-contg. peritrophic matrix surrounding the blood meal in the mosquito midgut. Since the peritrophic matrix is a phys. barrier that the parasite must cross to invade the mosquito, and the presence of allosamidin, a **chitinase** inhibitor, in a blood meal prevents the parasite from invading the midgut epithelium, **chitinases** (3.2.1.14) are potential targets of malaria parasite transmission-blocking interventions. We have purified a **chitinase** of the avian malaria parasite **Plasmodium** gallinaceum and cloned the gene, PgCHT1, encoding it. PgCHT1 encodes catalytic and substrate-binding sites characteristic of family 18 glycohydrolases. Expressed in Escherichia coli strain AD494 (DE3), recombinant PgCHT1 was found to hydrolyze polymeric chitin, native chitin oligosaccharides, and 4-methylumbelliferone derivs. of chitin oligosaccharides. Allosamidin inhibited recombinant PgCHT1 with an IC50 of 7 .mu.M and differentially inhibited two chromatog. separable P. gallinaceum ookinete-produced **chitinase** activities with IC50 values of 7 and 12 .mu.M, resp. These two **chitinase** activities also had different pH activity profiles. These data suggest that the P. gallinaceum ookinete uses products of more than one **chitinase** gene to initiate mosquito midgut invasion.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 2000:776463 CAPLUS
DOCUMENT NUMBER: 134:53651
TITLE: Micronemal transport of **Plasmodium** ookinete **chitinases** to the electron-dense area of the apical complex for extracellular secretion
AUTHOR(S): Langer, Rebecca C.; Hayward, Rhian E.; Tsuboi, Takafumi; Tachibana, Mayumi; Torii, Motomi; **Vinetz, Joseph M.**
CORPORATE SOURCE: World Health Organization Collaborating Center for Tropical Diseases, Department of Pathology, University of Texas Medical Branch, Galveston, TX, 77555-0609, USA
SOURCE: Infection and Immunity (2000), 68(11), 6461-6465
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Plasmodium** ookinetes secrete **chitinases** to penetrate the acellular, chitin-contg. peritrophic matrix of the

mosquito midgut en route to invasion of the epithelium. **Chitinases** are potentially targets that can be used to block malaria transmission. We demonstrate here that **chitinases** of **Plasmodium falciparum** and P. gallinaceum are concd. at the apical end of ookinetes. The **chitinase** PgCHT1 of P. gallinaceum is present within ookinete micronemes and subsequently becomes localized in the electron-dense area of the apical complex. These observations suggest a pathway by which ookinetes secrete proteins extracellularly.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:17983 BIOSIS
DOCUMENT NUMBER: PREV200100017983
TITLE: Identification of a novel secretory structure in **Plasmodium** ookinetes by a monoclonal antibody that recognizes a neutralization-sensitive epitope of **Plasmodium chitinases**.
AUTHOR(S): Langer, R. C. (1); **Vinetz, J. M. (1)**
CORPORATE SOURCE: (1) WHO Center for Tropical Diseases, University of Texas Medical Branch, Galveston, TX USA
SOURCE: American Journal of Tropical Medicine and Hygiene, (March, 2000) Vol. 62, No. 3 Supplement, pp. 205-206. print.
Meeting Info.: 49th Annual Meeting of the American Society of Tropical Medicine and Hygiene Houston, Texas, USA October 29-November 02, 2000 American Society of Tropical Medicine and Hygiene
. ISSN: 0002-9637.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L13 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 9
ACCESSION NUMBER: 1999:767999 CAPLUS
DOCUMENT NUMBER: 132:89991
TITLE: The **chitinase** PfCHT1 from the human malaria parasite **Plasmodium falciparum** lacks proenzyme and chitin-binding domains and displays unique substrate preferences
AUTHOR(S): **Vinetz, Joseph M.**; Dave, Sanat K.; Specht, Charles A.; Brameld, Kenneth A.; Xu, Bo; Hayward, Rhian; Fidock, David A.
CORPORATE SOURCE: WHO Center for Tropical Diseases, University of Texas Medical Branch, Galveston, TX, 77555, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1999), 96(24), 14061-14066
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Within hours after the ingestion of a blood meal, the mosquito midgut epithelium synthesizes a chitinous sac, the peritrophic matrix. **Plasmodium** ookinetes traverse the peritrophic matrix while escaping the mosquito midgut. **Chitinases** (EC

3.2.1.14) are crit. for parasite invasion of the midgut: the presence of the **chitinase** inhibitor, allosamidin, in an infectious blood meal prevents oocyst development. A **chitinase** gene, PgCHT1, recently has been identified in the avian malaria parasite P. gallinaceum. We used the sequence of PgCHT1 to identify a P. **falciparum chitinase** gene, PfCHT1, in the P. **falciparum** genome database. PfCHT1 differs from PgCHT1 in that the P. **falciparum** gene lacks proenzyme and chitin-binding domains. PfCHT1 was expressed as an active recombinant enzyme in Escherichia coli. PfCHT1 shares with PgCHT1 a substrate preference unique to **Plasmodium chitinases**: the enzymes cleave tri- and tetramers of GlcNAc from penta- and hexameric oligomers and are unable to cleave smaller native chitin oligosaccharides. The pH activity profile of PfCHT1 and its IC50 (40 nM) to allosamidin are distinct from endochitinase activities secreted by P. gallinaceum ookinetes. Homol. modeling predicts that PgCHT1 has a novel pocket in the catalytic active site that PfCHT1 lacks, which may explain the differential sensitivity of PfCHT1 and PgCHT1 to allosamidin. PfCHT1 may be the ortholog of a second, as yet unidentified, **chitinase** gene of P. gallinaceum. These results may allow us to develop novel strategies of blocking human malaria transmission based on interfering with P. **falciparum chitinase**.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:503731 BIOSIS
DOCUMENT NUMBER: PREV199900503731
TITLE: Biological characterization of a **Plasmodium falciparum chitinase**, a target of blocking malaria transmission.
AUTHOR(S): **Vinetz, J. M. (1)**; Specht, C. A.; Dave, S. K.; Fidock, D. A.; Hayward, R. E.; Langer, R. C.
CORPORATE SOURCE: (1) WHO Center for Tropical Diseases, University of Texas Medical Branch, Galveston, TX USA
SOURCE: American Journal of Tropical Medicine and Hygiene, (Sept., 1999) Vol. 61, No. 3 SUPPL., pp. 369. Meeting Info.: 48th Annual Meeting of the American Society of Tropical Medicine and Hygiene Washington, D.C., USA November 28-December 2, 1999 American Society of Tropical Medicine and Hygiene . ISSN: 0002-9637.
DOCUMENT TYPE: Conference
LANGUAGE: English

L13 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 10
ACCESSION NUMBER: 1998:702998 CAPLUS
DOCUMENT NUMBER: 130:77782
TITLE: **Plasmodium** gallinaceum: use of antiserums to degenerate synthetic peptides derived from the active site of protozoal **chitinases** to characterize an ookinete-specific **chitinase**
AUTHOR(S): **Vinetz, Joseph M.**; Kaslow, David C.
CORPORATE SOURCE: Malaria Vaccines Section, Laboratory of Parasitic Diseases, National Institute of

Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, 20892-0425, USA
SOURCE: Exp. Parasitol. (1998), 90(2), 199-202
CODEN: EXPAAA; ISSN: 0014-4894
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors hypothesized that the amino acid sequence of the active site of P. gallinaceum **chitinase** would be similar to the amino acid sequence of other protozoal, nematode, and higher bacterial **chitinases** and designed synthetic peptides based upon these sequences. Degenerate and nondegenerate synthetic peptides based upon the active sites of other protozoal **chitinases** generated antisera that detected a .apprx.50-kDa ookinete stage-specific protein. Antisera that recognized the E. hystolytica **chitinase** active-site immunoeluted a protein with **chitinase** activity from P. gallinaceum ookinete exts.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:473981 BIOSIS
DOCUMENT NUMBER: PREV199799773184
TITLE: Biochemical and immunological characterization of a **Plasmodium chitinase**, a malaria transmission-blocking vaccine candidate.
AUTHOR(S): **Vinetz, Joseph**; Kaslow, David
CORPORATE SOURCE: NIH, Bethesda, MD USA
SOURCE: Clinical Infectious Diseases, (1997) Vol. 25, No. 2, pp. 428.
Meeting Info.: 35th Annual Meeting of the Infectious Diseases Society of America
ISSN: 1058-4838.
DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

L13 ANSWER 14 OF 14 CONFSCI COPYRIGHT 2002 CSA
ACCESSION NUMBER: 2000:70541 CONFSCI
DOCUMENT NUMBER: 00-067412
TITLE: Identification of a novel secretory structure in **Plasmodium** ookinetes by a monoclonal antibody that recognizes a neutralization-sensitive epitope of **Plasmodium chitinases**
AUTHOR: Langer, R.C.; **Vinetz, J.M.**
CORPORATE SOURCE: WHO Cent. for Tropical Diseases, Univ. Texas Med. Branch, Galveston, TX, USA
SOURCE: American Society of Tropical Medicine and Hygiene, 3088 Briarcliff Rd., Ste. 11A, Atlanta, GA 30329, USA

Meeting Info.: 000 5172: ASTMH 49th Annual Meeting (0005172). Houston, Texas (USA). 29 Oct-2 Nov 2000. American Society of Tropical Medicine and Hygiene.
DOCUMENT TYPE: Conference
FILE SEGMENT: DCCP
LANGUAGE: English

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, USPATFULL' ENTERED AT 10:53:41 ON 29 MAR 2002)

L14 21 S VINETZ J?/AU AND L6
L15 0 S L14 NOT L12

FILE 'HOME' ENTERED AT 10:54:16 ON 29 MAR 2002